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THE MEASUREMENT OF THE CARDIAC OUTPUT: AN INVESTIGATION OF THE CARBON DIOXIDE METHOD.

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THE cardiac output—that is to say, the volume of blood pumped out by the heart in one minute—can be determined in various ways, most methods depending on the application of Fick's principle. In applying this principle it is necessary to estimate the arterio-venous difference for oxygen or for carbon dioxide and the corresponding gaseous exchange. The main difficulties are met with in the determination of the arterio-venous difference, and an article has already been published in this journal summarizing the difficulties encountered in the application of the foreign gas method to this determination.

It is not practicable, because of the risks involved, to apply the Fick principle directly by means of heart puncture to clinical subjects, and so recourse has been had to various indirect methods for the determination of the arterial and venous levels of oxygen and carbon dioxide.

Loewy and von Schrötter,[(1)] by means of a bronchial catheter provided with an inflatable rubber ring, succeeded in isolating a portion of the lung from the general respiratory cycle. Samples of the gas from this section of the lung were withdrawn and analysed from time to time, and it was observed that the tensions of the oxygen and carbon dioxide finally became constant, this fact indicating that equilibrium between the gas in the alveoli and in the venous blood had been reached. The subject's blood was then equilibrated with gas of the composition as above determined and analysed for gaseous content. This gave the figures for venous oxygen and carbon dioxide content. The subject's blood was next equilibrated with gas corresponding in composition to the alveolar air, and this, on analysis, gave the figures for the gaseous content of the arterial blood. The arterio-venous difference as above determined divided into the gaseous exchange gave the cardiac output.

All methods based on the indirect application of Fick's principle have this in common with Loewy and von Schrötter's method—namely, that they require the exact determination of the venous and arterial levels of either oxygen or carbon dioxide; but Loewy and von Schrötter's method has the disadvantage that it cannot be used as a routine procedure on clinical subjects, since it involves an unpleasant and complicated procedure which in itself may disturb the psychic state of the patient, with consequent elevation of the cardiac output. Therefore, the general basis for these indirect methods is some rebreathing procedure for the determination of the venous levels, coupled with the direct estimation of the gaseous content of the alveolar air. The figures so obtained are applied to a dissociation curve in order to determine the gaseous content of the blood. Sometimes arterial puncture is substituted for the taking of alveolar samples; but it is not possible to substitute venipuncture for the indirect determination of the gases in the mixed venous blood because of the great variation in gaseous content from vein to vein.

Arterial puncture must give precise figures, within the limits of experimental error in analysis, for the gaseous content of arterial blood; but owing to its being painful for the subject, it may result in a reflex increase in the depth and rate of respiration, which will produce a greater oxygen saturation and a lower carbon dioxide content in the arterial blood than that found in the subject when undisturbed by such a procedure.

Since, as Meakins and Davies[(2)] pointed out, arterial puncture generally causes spasm of the artery which lasts for ten to fifteen seconds, during which time the vessel is quite pulseless and incapable of yielding any blood, there is a considerable time for any change in the respiratory cycle to make itself shown in the arterial blood.

Though these changes are likely to be small and to affect the carbon dioxide content more than the oxygen content, yet the question is raised whether the figures for gaseous content obtained by direct analysis are any closer to the normal resting values than those obtained indirectly from the alveolar gas tensions.

There has been much discussion in the literature concerning the relationship between the tension of the gases in the alveoli and the tensions in the capillaries which supply these alveoli. So far as carbon dioxide is concerned, it was asserted as far back as 1910 by Krogh[17] that "the mean alveolar tension and the tension in the arterial blood must be practically identical within the limits of experimental error". Krogh defines the diffusion constant of a gas in the physiological sense as "the number of c.c. of the gas which will, in one minute, diffuse through a distance of 1μ (0·001 mm.) over an area of one square centimetre when the concentration difference corresponds to one atmosphere". Hüfner, quoted by Krogh, in 1897 had found this constant for oxygen in water to be 0·34. Krogh determined the constant for connective tissue and oxygen at 20° C. and found it to be 0·115. He considered that for carbon dioxide in tissues it was some thirty times higher than for oxygen. Bohr (1905) investigated the absorption coefficient of oxygen in blood at 38° C. and found it to be 0·022 and for carbon dioxide in the same circumstances the constant was 0·511, a value some twenty-five times as great.

Recent work by Josselyn[18] suggests that, in the lungs, the alveolar lining may be a discontinuous membrane and the capillaries in some sections are uncovered, the alveolar air thus being separated from the capillary blood by only a layer of endothelium. Carbon dioxide is known to cause the opening up of the capillary bed, and the venous blood returning to the lungs has a gaseous content ideally suited for keeping the pulmonary alveolar bed at an optimum, thus maintaining the most intimate relation between the alveolar air and the blood.

Plesch[21] holds that the flow of blood through any patent capillary is turbulent, and this in itself would tend to prevent the more central part of a capillary from possessing a physical state much different from its periphery, for the mechanical agitation of the capillary contents by the streaming corpuscles removes from contact with the capillary wall that plasma which is already in gaseous equilibrium with the alveolar air, replacing it with plasma not yet in this state, so that by the time the distal end of the capillary is reached all of its contents (and not merely its outermost portion) has been in intimate contact with the alveolar air across the capillary endothelium. Furthermore, this turbulence causes a continual changing of the plasma in contact with the individual corpuscles, through the walls of which oxygen must diffuse inwards and carbon dioxide outwards. Thus the general direction of the physical factors governing the gaseous exchange is towards the production of a state of equilibrium between the gas tensions of the blood of the distal end of the capillaries and the alveoli. The rate at which this equilibrium is reached is, for carbon dioxide, enormously quickened by the presence of the enzyme carbonic anhydrase within the red corpuscle, as shown by Brinkman, Margaria, Meldrum and Roughton[4] and by Meldrum and Roughton.[28] This catalyses the following reaction:

$$H_2CO_3 \rightleftharpoons H_2O + CO_2$$

Roughton pointed out that in order to meet physiological requirements the above reaction would need to be accelerated 150 times, and there is enough enzyme in the blood of normal subjects to accelerate this reaction some 1,500 times. Moreover, as has been shown by Lambie,[26] the amount of enzyme present is not reduced to dangerous levels even in the blood of subjects of profound anæmias. Indeed, in macrocytic anæmias the concentration of the enzyme in each cell is increased; this compensates for the smaller number of circulating cells. The same author[23] has pointed out that in microcytic anæmias the gaseous exchange between plasma and corpuscles is greatly facilitated by the relatively greater surface to volume ratio of the cells and by the shorter distance through which the gases diffuse in the cells.

The evidence, as far as the normal healthy lung is concerned, is overwhelmingly in favour of the conclusion of Krogh and Lindhard[19] that "the blood leaving the lungs is in practical carbon dioxide tension equilibrium with the alveolar air, as shown experimentally by A. and M. Krogh, while the oxygen pressure of the alveolar air constitutes the limit to which the arterial blood can attain by diffusion".

Small, though persistent, variations in the alveolar gas tensions in the one subject at the one sitting have been noted by most observers. The method of Haldane and Priestley[14] of determining the alveolar air, though simple in principle, requires cooperation and concentration from the subject, who must, at the end of either a normal inspiration or an expiration, breathe out forcibly through a long rubber hose and seal the proximal end with his tongue whilst the sample is taken. There is a tendency, even among subjects accustomed in some measure to the procedure, to preface the forcible expiration from which the samples are taken, with an abnormally deep inspiration, thereby diluting the alveolar air with an unknown amount of inspired air. Such an occurrence quite invalidates the figures obtained, which, compared with the true resting values, would be too low for carbon dioxide and too high for oxygen. Criticism has also been levelled against the results obtained by the Hasselbalch-Lindhard method of obtaining alveolar samples; this method seeks to trap the terminal portion of each expiration. It has been urged that a normal expiration is not sufficient in volume adequately to wash out the pulmonary dead space; but Debenham and Poulton[12] dispute this and maintain that the two methods give comparable results. Bock and Field[5] have checked the Haldane-Priestley method against direct analysis of the arterial blood and have shown that for "end of expiration" samples there is little variation between the alveolar and arterial gas tensions. Dautrebande,[6] taking the mean of "inspiratory" and "expiratory" samples and comparing them with the gaseous tensions of the arterial blood as determined by direct analysis, has demonstrated a remarkable concordance even among abnormal subjects.

Alveolar tensions, by whatever method determined, have been shown to vary amongst themselves even in perfectly trained subjects at rest when multiple estimations have been performed on the same day. If the possibility of serious experimental error is eliminated, the question arises as to whether these variations mean that, although the gaseous tensions of the arterial blood remain constant, they bear a measurable, though variable, relation to the gas tensions in the alveoli, or whether there is indeed a variability in the gaseous content of the venous blood coming to the lungs, which reflects itself in a change in the arterial gas tensions, causing in turn a change in the observed alveolar tensions.

Table I, from Haldane and Priestley's "Respiration", shows variations of alveolar carbon dioxide tension over a period of some twenty months in the one subject (J.S.H.) at rest. It will be seen that for "end of inspiration" samples there is a variation from 37·2 millimetres to 40·7 millimetres, which is 9% of the mean value—namely, 39·0 millimetres—and for the "end of expiration" samples the variation is from 38·5 millimetres to 41·7 millimetres, which is 8% of the mean value—namely, 40·3 millimetres. Similar variations can be noted in the published work of many other observers—for example, Wardlaw[31] and Debenham and Poulton[12]—and it is now generally accepted that the alveolar carbon dioxide tension is extremely labile, not only from day to day, but from minute to minute.

Hasselbalch, quoted by Haldane and Priestley,[14] had found that the resting alveolar carbon dioxide tension was higher by some 4·5 millimetres when the subject was taking a vegetable diet than when he was taking a meat diet, and this could account for variations observed over a moderately long period of time.

Dodds[11] and Bennett and Dodds[2] investigated the effect of meals on the alveolar air and observed that the carbon dioxide tension rose immediately after a meal,

TABLE I.[1] [2]
"J.S.H."

Bar.	Carbon Dioxide. (Percentage.) End of Inspiration.	Carbon Dioxide. (Percentage.) End of Expiration.	Carbon Dioxide. (Percentage.) Mean.	Carbon Dioxide. (Millimetres.) End of Inspiration.	Carbon Dioxide. (Millimetres.) End of Expiration.	Carbon Dioxide. (Millimetres.) Mean.
759	5·33	5·76	5·545	37·9	40·9	39·4
747	5·47	5·69	5·56	38·2	39·7	38·8
748	5·56	5·70	5·63	38·9	39·9	39·3
748	5·59	5·87	5·73	39·0	41·0	40·1
748	5·38	5·60	5·49	37·6	39·1	38·4
748	5·33	5·94	5·40	37·2	41·5	39·35
749	5·80	5·51	5·87	40·6	38·5	39·6
749	5·66	5·59	5·585	39·6	39·1	39·35
765	5·63	5·83	5·61	40·3	41·7	41·0
759	5·42	5·72	5·625	38·5	40·6	39·9
758	5·74	5·72	5·71	40·7	40·6	40·7
765	5·53	5·72	5·62	39·6	41·0	40·2

[1] After Haldane and Priestley, "Respiration", page 21. (Gas tensions in millimetres have been calculated.)

[2] The figures are as quoted in "Respiration"; but some discrepancy is observable in the computation of the mean—for example, the mean of 5·33 and 5·94 is given as 5·40.

coincidentally with a rise in the gastric hydrochloric acid. This rise amounted to about 4·0 millimetres of mercury, and about two hours after a meal there was a corresponding fall below normal. Main[24] found considerable variations in the alveolar carbon dioxide tensions of fasting subjects, generally at the accustomed meal hour, and these, he thinks, are due rather to respiratory stimulation caused by hunger contractions than to the secretion of gastric juice, for he noticed that when the subject was given only a biscuit the variations, though still present, were much less in extent. Barcroft and Robinson[1] observed that the exteriorized intestine was quite active even in the fasting animal, and peristaltic movements would, of course, influence the carbon dioxide production. Main[25] has also found that the alveolar carbon dioxide tension in the erect subject is lower than in the recumbent subject; he attributes this fact to pulmonary hyperventilation caused by stimulation of the respiration by the cephalic ischæmia resulting from the assumption of the erect position.

Thus it can be seen that there is much evidence to support the belief that the apparent lability of the alveolar gas tensions, at any rate as far as carbon dioxide is concerned, is real and not the result of experimental error, and furthermore, that the observed tensions approximate very closely to the tensions in the blood leaving the pulmonary capillaries. There is evidence, too, to show that in the basal state there exists a complex of physiological factors, inconstant in direction, modifying the gaseous content of the venous blood, which also can be demonstrated to have a fluctuant value. For example, bowel movements or the secretion of a few drops of hydrochloric acid in the stomach will cause the carbon dioxide level in the venous blood to rise, and this blood is aerated in the lungs by a rate and depth of respiration conditioned by the response of the respiratory centre to the carbon dioxide content of the blood which has already passed through the lungs, having by hypothesis a lower carbon dioxide content. This blood, which had the higher venous content of carbon dioxide, will after aeration leave the lungs with a higher carbon dioxide content than the blood immediately before it, and will in turn influence the respiratory centre when other blood, which may indeed now contain a lower venous level of carbon dioxide, is being aerated. The hyperventilation produced will cause this blood leaving the pulmonary capillaries to have a lower carbon dioxide content, and when this blood reaches the respiratory centre it will cause a diminution of its activity.

Besides these changes in the "internal environment", the changes in the alveolar tensions corresponding to the inspiratory and expiratory phases of respiration are reflexes of the corresponding changes in the arterial tensions, which in turn depress and stimulate the activity of the respiratory centre. The respiratory "picture" is an intensely individual thing, as can be seen from an inspection of the graphs from either a Krogh or a Sanborn metabolimeter; but it is found that the expiratory level is generally more constant than the inspiratory level, and this may account for the greater constancy and reliability claimed for "end of expiration" samples. This claim is reinforced by the fact that by far the longer period of the respiratory cycle is spent in the expiratory phase, if the pause which succeeds each expiration at rest is included. Owing to the exquisite sensitivity of the respiratory centre combined with its anatomical remoteness from the lungs, the gaseous tensions in the blood are not static, but are continuously fluctuating, now above, now below, the mean value. This does not mean that the mean value is unobtainable, for in doubtful cases it can be determined by averaging a sufficient number of samples taken at various phases of respiration.

The determination of the gaseous tensions of the mixed venous blood is not an easy matter. Loewy and von Schrötter[29] succeeded, as has been mentioned above, by shunting a portion of the lung from the general respiratory cycle and waiting for the attainment of equilibrium in the gases of the occluded space. Plesch[30] sought to use the whole of the lungs as such a closed system, and he introduced the rebreathing procedure for the estimation of the venous tensions. This has become the basis for all subsequent indirect methods. In its application to the determination of the cardiac output his method, briefly stated, was to rebreathe in and out of a rubber bag a gas mixture approximating the gas tensions of the mixed venous blood. When it was deemed that equilibrium had been reached, the values obtained by analysis were applied to a dissociation curve and the volumes *per centum* of gas read off. The figures for the arterial oxygen content were obtained by equilibration *in vitro* of a sample of blood with air followed by direct analysis. Plesch's results for cardiac output for normal individuals are approximately correct, being between three and five litres, with a stroke volume of about 60 cubic centimetres. These results are perhaps a little fortuitous in their apparent correctness, for they depend on the accurate estimation of the venous oxygen tension, which is still a notoriously difficult procedure. Moreover, no special care was taken to maintain basal conditions in the subjects, and often the rebreathing time greatly exceeded the circulation time, which would mean that the gaseous equilibrium would be obtained not with the "resting" mixed venous blood, but with blood having less oxygen and more carbon dioxide than this, owing to recirculation.

Christiansen, Douglas and Haldane[31] (1914) found that the carbon dioxide tension of the venous blood depended upon the state of oxygenation of the blood; that is to say, a given sample of blood, its content of carbon dioxide being maintained constant, would have a much higher carbon dioxide tension when oxygenated than when reduced (Figure I). They observed that, no matter for how long a sample of air was rebreathed, the carbon dioxide tension never became constant; this indicated that the rebreathed gas had never attained equilibrium with the venous blood. This was because there was never sufficient carbon dioxide present to achieve this equilibrium within the period of time allowed for one circulation. They therefore tried breathing mixtures of air to which carbon dioxide, varying

between 5% and 15%, had been added. The technique was to take a maximal inspiration of such a mixture, hold it in the lungs for five seconds and then expire about a litre. A sample was taken at this point and after a further four seconds another litre was expired and another sample taken. Yet another sample could be taken after another four seconds if deemed necessary. If the carbon dioxide tension increased from sample to sample, it was inferred that the venous level was somewhat higher than that shown in the last sample. If the samples showed a continual decrease, the inference was that the venous level was somewhat below that of the last sample. When two successive samples agreed, or almost agreed, the mean was taken to represent the venous level uncorrected for oxygenation. The technique, as described, was long and cumbrous, and even with a trained subject three out of four experiments were abortive. The method of partial expiration followed by alveolar sampling is one that cannot be applied to clinical investigation, since it requires the utmost cooperation and concentration on the part of the subject. Furthermore, as Douglas and Haldane[32] later pointed out, a single deep breath is not sufficient to bring about gaseous homogeneity in the lungs, so that it was possible for an apparent agreement between successive samples to be fortuitous and unreal.

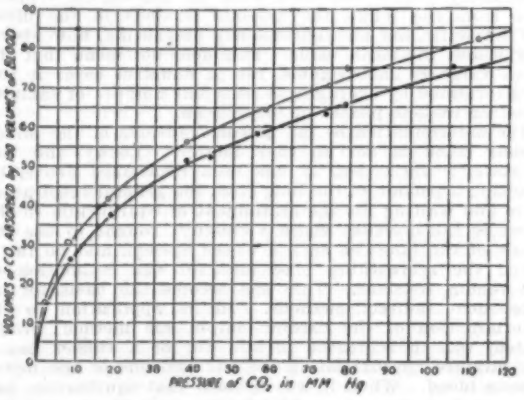

FIGURE I.

Lower curve: absorption of carbon dioxide by blood of J.S.H. in presence of air and carbon dioxide. Upper curve: absorption of carbon dioxide by blood of J.S.H. in presence of hydrogen and carbon dioxide. (From Haldane and Priestley, "Respiration".)

These authors sought to arrive at the true venous gas tensions by washing out the lungs with a mixture which approximated, in composition, to the tensions expected. The breath was then held for two seconds and a sample was taken after a partial expiration; after another five seconds, during which the breath was held, the expiration was completed and another sample was taken. When successive samples showed agreement, it was assumed that gaseous equilibrium had been reached between the venous blood and the alveolar air, and the values obtained were applied to the corresponding dissociation curve corrected for observed respiratory quotient. The alveolar tensions during the breathing of air, on being applied to the dissociation curve, gave the gaseous content of the arterial blood. The difference between the arterial and venous tensions, when divided into the respiratory exchange, gives the cardiac output. The values obtained varied from five to eight litres, and were somewhat higher, in the light of more recent evidence, than should have been the case for resting subjects. This is probably due to a number of factors, including the non-insistence on strictly basal conditions and the difficulty of applying the correction for respiratory quotient, which, compared with its resting value, must change considerably during the course of such an experiment. Indeed, if true equilibrium is reached between the gases of the alveoli and the venous blood, then at that instant, since there is neither excretion of carbon dioxide nor absorption of oxygen, the respiratory quotient must be zero.

Henderson and Prince (1917) tried the intermittent rebreathing of expired air for periods of up to fifteen seconds, and they observed that somewhere about the seventh rebreathing, the carbon dioxide content in the bag reached a steady value, which they assumed to be the venous level. If the bag at the commencement of the rebreathing period contained air to which 9% of carbon dioxide had been added, it was found that the content of this gas fell until it equalled the value obtained from the rebreathing of expired air (Figure II).

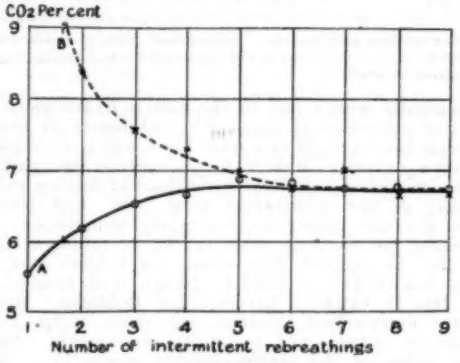

FIGURE II.

In this diagram the numbers on the abscissa represent successive rebreathings at intervals sufficient for return of normal breathing. Curve A: Beginning with a full expiration into the bag, each observation thereafter represents the carbon dioxide percentage obtained by rebreathing the contents of the bag only once (inspiration five seconds, expiration five seconds). Curve B: Beginning with inspiration of an artificially prepared 10% carbon dioxide mixture in the bag, the succeeding observations were made as in the case of curve A. It will be noted that after the sixth intermittent breath the carbon dioxide in the bag is in equilibrium with the venous carbon dioxide tension. (From Henderson and Prince, *Journal of Biological Chemistry*, Volume XXXII, 1917.)

Meakins and Davies[28] also used the intermittent rebreathing method. A rubber bag of some five litres' capacity was filled with expired air containing about 5% of carbon dioxide. The subject breathed deeply in and out of this bag twice in a period not exceeding fifteen seconds. Then after a short interval the procedure was repeated, and so on, until after the fifth to seventh rebreathing agreement in carbon dioxide content of the samples taken at the end of the rebreathing periods was observed. The tension so observed was taken to be in equilibrium with the mixed venous blood and was applied to the dissociation curve of Christiansen[6] in order to convert the result to volumes *per centum*. The carbon dioxide in the alveolar air was also determined and applied to the curve, the difference being the arterio-venous carbon dioxide difference. The method was very time-consuming and required a large number of rebreathings, from each of which a gas sample was analysed, and it gave values for cardiac output in the resting subject ranging from 7·27 to 8·4 litres per minute. Apparently some of the rebreathings, even after the fifth, were abortive, for only some and not the whole of them were averaged in order to obtain the tension in the mixed venous blood. This figure, it seems, was applied to the dissociation curve in fully oxygenated blood, whereas the blood, having been aerated with rebreathed expired air, could have been only partially saturated with oxygen. Thus the value for volumes *per centum* of carbon dioxide in the venous blood was too low, in turn causing the arterio-venous difference to be too small and the cardiac output to be too high.

Liljestrand and Lindhard[22] had attempted to find the gaseous tensions in the venous blood by the method of

Frederica. This method was as follows: a deep breath of a mixture of carbon dioxide and air, which was sometimes enriched with oxygen, was taken from a spirometer, the breath was held in the lungs for two or three seconds, and then half of the breath was expired to the spirometer, whereon a sample was taken. After seven to ten seconds the rest of the air was expired and another sample was taken. The procedure was repeated a large number of times, and from the results the venous carbon dioxide tension was inferred. The alveolar carbon dioxide tension was not determined directly, but was calculated from respiratory data. Liljestrand and Lindhard did point out, as had already been suggested by Hasselbalch, that not only the height but the shape of the carbon dioxide dissociation curve varied from subject to subject (Figure III). They determined the curve for each subject and applied their venous and arterial tensions to these curves, obtaining an arterio-venous difference in each case of 5·2 volumes *per centum* and a cardiac output in one subject of 3·6 litres per minute and in the other of 3·3. These figures are somewhat low, and the source of error is probably the low values obtained for alveolar carbon dioxide tension, which would cause the arterio-venous difference to be too great, as indeed is the case. The method, too, meets with the common criticism that it is too long and too specialized in character for general application.

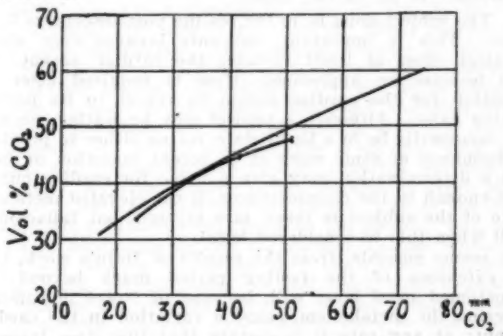

FIGURE III.

Upper curve: absorption of carbon dioxide by blood of G.L. in presence of oxygen and carbon dioxide (37° C.). Lower curve: absorption of carbon dioxide by blood of J.L. in presence of oxygen and carbon dioxide (37° C.). (From Liljestrand and Lindhard, *The Journal of Physiology*, Volume LIII, 1919.)

Burwell and Robinson[5] combined the "washing out" procedure with the rebreathing procedure to arrive at the true gaseous tension of the venous blood. The washing out mixture consisted of about 7% carbon dioxide in nitrogen, which was twice rebreathed from a large spirometer and then back and forth into a rubber bag during another three breaths. The subject was then switched to air, and after an interval the procedure was repeated from seven to eleven times, a sample for analysis being taken from the bag after each rebreathing. After a varying number of rebreathings, fewer in the case of carbon dioxide than in that of oxygen, the gas tensions from successive samples became constant at the venous level, and the subject's blood was equilibrated with gas of this composition and analysed. The gaseous content of the arterial blood was determined by direct analysis. The arterio-venous difference so obtained was in the two cases of the right order, as was also the cardiac output; but the method, in common with most of the others described, is long, very involved and not suitable for application to hospital patients, for, as Burwell and Robinson state, "the subject is fairly dyspnœic for five or six breaths after the rebreathing and may shew moderate cyanosis, but there is no change in heart rate". The method has been tried in this laboratory on subjects accustomed to such procedures; their reaction to the partial asphyxia involved was profound, and entailed almost certainly an increase in cardiac output immediately after the experiment, if not during it, in order quickly to compensate for the oxygen want produced. The psychic state of the subject is also disturbed, and this by itself, as Grollman has pointed out, would tend to increase the output of the heart. It would probably require a moderate length of time for the effects of the disturbance, psychical and organic, to wear off, particularly so in the case of clinical subjects, and this must greatly prolong the time between rebreathings and hence the total time of the whole experiment. In the case of subjects already suffering from serious cardiac disorder there is the possibility of damage resulting from the sudden strain in the post-rebreathing "recovery" period. Probably for these reasons the method has not had much application as a routine procedure in the investigation of hospital patients, although, in selected normal subjects, as Burwell and Robinson[5] have shown in another paper, it is capable of yielding fairly accurate results. However, in two of the eleven cases grossly elevated values for cardiac output were obtained, and they themselves were unable to detect any relationship between cardiac output and surface area—a relationship which is now well recognized.

Field, Bock, Gildea and Lathrop[13] employed the rebreathing method and substituted a mixture of 6% carbon dioxide in oxygen for expired air, seeking by this means to obtain the carbon dioxide tension of the venous blood, which had been oxygenated, but from which no carbon dioxide had been allowed to escape. They observed that the tensions so obtained were invariably 0·5 to 1·0 millimetres of mercury higher than those obtained when expired air was rebreathed, and they rightly attributed this to incomplete oxygenation of the blood in the latter case. They noted that the oxygen saturation of the blood was apparently complete at an oxygen tension of about 150 millimetres of mercury, for when this value was greatly exceeded there was no rise in the observed carbon dioxide tension. From Table II, which is from their paper, it can also be seen that the level of the venous carbon dioxide tension shifts considerably from time to time. This fact was commented on by Field and his colleagues and they devised a system of taps, whereby immediately after the taking of an alveolar sample the subject was changed over to the rebreathing system, into which he respired for about fifteen seconds; at the end of this time a sample was taken. After multiple rebreathings the venous carbon dioxide tension was inferred. This was, of course, for oxygenated blood. The calculation of the cardiac output was made by the use of a factor corresponding to the slope of a standard dissociation curve within the tension range found, which was multiplied by the observed

TABLE II.

Experiment.	Gas Mixture after Rebreathing.	
	Dioxide Tension.	Carbon Dioxide Tension.
1	347	46·6
	268	46·15
	246	46·8
	184	46·55
2	308	47·9
	271	47·8
	197	48·6
	151	48·2
3	284	42·8
	259	43·0
	192	43·0
	174	42·7
4	423	44·1
	343	44·7
	232	46·4
	158	44·7

[1] From Field, Bock, Gildea and Lathrop.[13]

difference in carbon dioxide tension from which 1·0 millimetre had been subtracted. This subtraction was to compensate for the error due to the "small difference in CO_2 tension which probably exists between the alveolar air and arterial blood", and because the arterial blood is only 95% saturated with oxygen, while the blood from contact with the gas in the rebreathing bag would generally be almost completely saturated because of the high oxygen tension in the bag.

The arterio-venous differences for carbon dioxide calculated from the results of this method are, for the most part, much too low, and this is mainly due to the arbitrary subtraction of one millimetre from the observed tension difference. Indeed, Bock and Field showed that there was little difference between the carbon dioxide tension of the blood and of the alveoli and that it was far less than one millimetre of mercury.

It is not permissible to adopt a "standard" dissociation curve for carbon dioxide, because the shape and position of such a curve varies among different subjects, as Liljestrand and Lindhard[12] have pointed out. Figure IV shows a number of carbon dioxide dissociation curves determined in this department, and they reinforce this view.

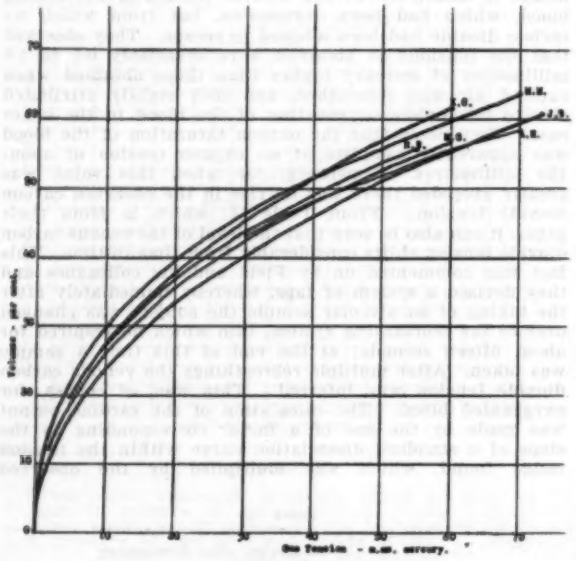

FIGURE IV.

Dissociation curves of carbon dioxide in the fully oxygenated blood of six subjects. The curves of the other four subjects are not reproduced, because they tend to duplicate some of the above.

Moreover, because the level of carbon dioxide in the venous blood changes from time to time even during rest, absolute agreement between samples from successive rebreathings is rare, and even if attained is still no guarantee that equilibrium between the bag contents and the blood has been reached. Approximate agreement, *a fortiori*, is open to a similar objection, and the most that can be said for the venous carbon dioxide tension determined by the analysis of single samples taken during a series of rebreathings, is that there is a strong probability, but no certainty, that it is near the correct value. In short, there is no internal check on the accuracy of the venous level determined by the method of multiple rebreathing.

Israëls and Lamb[13] confirmed the findings of Haldane *et alii* (1914) that insufficient oxygenation of the blood may cause a very much lower carbon dioxide tension to be observed in the rebreathing bag. They concluded that if the oxygen in the rebreathing bag was maintained at or above 26%, there was complete oxygenation of the blood and the observed carbon dioxide tension was stable at its maximal value. They pointed out that agreement between samples from successive rebreathings might be fallacious if taken uncritically as a criterion of the attainment of equilibrium between the carbon dioxide tension of the venous blood and the rebreathing bag. In this view Grollman concurred, and he put the matter succinctly thus:

> An observed constancy may, therefore, easily be deceptive and actually due to constant repetition of the same procedure rather than to attainment of true equilibrium.

Cooke and Priestley[7] compared the carbon dioxide method with the acetylene method, and devised a scheme by means of which both these methods could be applied simultaneously to the same patient. It is not stated in the paper how the carbon dioxide tensions were converted to volumes *per centum*, but it is assumed that a "standard" dissociation curve was used. They found approximate agreement between the two methods, the results from the acetylene method showing somewhat better agreement among themselves and being lower than those from the carbon dioxide method.

It is now appropriate to summarize the difficulties and necessary conditions underlying the carbon dioxide method. It will be seen that some of these are also common to the acetylene method and have already been mentioned in an earlier paper.

1. The subject must be in the resting post-absorptive basal state. This is important, not only because even slight physical effort of itself elevates the cardiac output, but also because an appreciable time is required after its cessation for the cardiac output to revert to its normal resting value. Although a subject may be resting, he may not necessarily be in a basal state, owing either to previous performance of some work or to recent ingestion of food, and a determination may give a value for cardiac output true enough in the circumstances, if the elevated metabolic state of the subject is taken into account, but fallaciously high when this is considered basal.

It seems possible, from the results of Main's work, that an extension of the fasting period much beyond the accustomed meal hour will, because of bowel movements affecting the metabolism, cause a variation in the cardiac output; at any rate it is certain that this does increase the lability of the carbon dioxide tension in the arterial blood as shown by analysis of the alveolar air. A state of psychic tranquillity should also be maintained in the subject.

Arterial puncture, though giving accurate figures for the carbon dioxide content of the blood, may cause reflex alteration of the rate and depth of respiration by the pain it occasions, even if it does not directly elevate the cardiac output, with the result that the values obtained are different from the resting values and thereby lead to an unreality in the apparent arterio-venous difference.

2. Accurate alveolar samples must be obtained. In the taking of alveolar samples as little as possible should be left to the cooperation or concentration of the subject, for as is well known, mere consciousness of one's breathing will alter its character. The Haldane-Priestley method, as usually applied, requires a fair degree of active cooperation from the subject, and this requirement considerably limits its scope. Perhaps the most common error to be met with is caused by the failure to make an expiratory effort of sufficient volume at the right instant, and this results in the supposedly alveolar air consisting of expired air from the dead space mixed with a variable proportion of true alveolar air. This results, in turn, in a fallaciously low alveolar carbon dioxide tension, which causes an increase in the apparent arterio-venous difference and a decrease in the calculated cardiac output.

There has been much discussion in the literature as to whether the gaseous tension of the arterial blood is represented most accurately by the sample taken at the end of a normal inspiration, by that taken at the end of a normal expiration, or by the mean of these two. It has been suggested by Bock and Field that those samples taken at the end of expiration are the best, because the time taken

by expiration permits diffusion within the alveoli to become more complete, and the sample taken at its end is therefore more representative of the gaseous environment in the pulmonary capillaries.

Inspiration causes the dilution of the gas in the alveoli with a variable amount of inspired air, and these authors state that "since the diffusion can hardly be instantaneous the air in an alveolus is probably never a uniform mixture during normal respiration. There is, in the centre, a comparatively large proportion of fresh air, while as the alveolar wall is approached the carbon dioxide content gradually increases and the oxygen content decreases." However, the time required for this diffusion, though not instantaneous, must be very short indeed, and it does tend to cause a fall and rise in the alveolar carbon dioxide tension corresponding with inspiration and expiration. At the same time, however, the fluctuation of carbon dioxide tension within the alveoli produces a change in the carbon dioxide tension of the blood leaving the pulmonary capillaries. The carbon dioxide tension of the alveoli is not only influenced by, but also influences, the tension in the pulmonary blood.

Thus, in the case of "end of inspiration" samples, because there is a dilution of the alveolar air with inspired air and because there is in the alveoli a greater volume of air into which the gas from the blood may diffuse, the carbon dioxide tension gradient between the blood and the alveoli increases and carbon dioxide is given off at a faster rate, and therefore its tension falls in the blood leaving the pulmonary capillaries. This tension, because of the high rate of diffusion of carbon dioxide, is very close indeed to that in the alveoli. Conversely, in "end of expiration" samples, because of the longer time which the alveolar air spends in the lungs, and because there is a smaller volume of alveolar air into which the gas from the blood may diffuse, the carbon dioxide tension gradient between the blood and the alveoli falls, carbon dioxide is given off at a slower rate, and therefore its tension rises in the blood leaving the capillaries and hence in the alveoli. The point which is here made is that the carbon dioxide tension of the blood leaving the pulmonary capillaries has not a static value, but fluctuates up and down with expiration and inspiration, and the observed carbon dioxide tension in the alveolar air does approximate, more or less closely, to the tension occurring in the blood at the instant when such samples are taken.

The lability of the alveolar carbon dioxide level, and hence of the arterialized blood in the lungs, under the influence of work, of change of type of diet, of secretion of gastric hydrochloric acid, of fasting and of change of posture, has already been noted by Haldane and Priestley,[24] by Hasselbalch,[10] by Bennett and Dodds,[3] and by Main,[20][23] and now we have to add to these the rhythmic rise and fall corresponding to the phases of respiration. However, the small differences, due to respiratory causes, in the carbon dioxide tension of the blood leaving the pulmonary capillaries will be much diminished by the time the blood reaches the respiratory centre because of the mixing produced by the action of the left side of the heart.

It seems, as Bock and Field[3] and others have held, that "end of expiration" samples more accurately correspond with the tension of the mixed arterial blood than "end of inspiration" samples or the mean of the two, not only because there has been a longer time for equilibrium between the blood and the alveoli to take place (for, as far as carbon dioxide is concerned, this must be reached very quickly indeed), but because in most resting subjects a longer time is spent in the expiratory than in the inspiratory phase of respiration. In a variable system such as this, the average tension would best be obtained by taking the mean of a large number of points, equally spaced in time, and because the expiratory phase is longer than the inspiratory phase, this mean will lie nearer to the expiratory extreme. However, in the case of those subjects in whom the two phases are of equal length, the mean of a large number of points would be equal to the arithmetical mean of the extremes. Thus, whatever point is taken as representing the "mixed" arterial blood, it can be accurately determined only by reference to the "respiratory picture" of the subject concerned. It is also an advantage if some internal check can be applied to the samples taken to detect contamination through insufficiently deep expiratory effort of the alveolar air with air from the dead spaces.

3. The venous level of the carbon dioxide must be accurately known. Heart puncture, with due precaution to avoid disturbance of the subject, will give this value by direct analysis of the blood; but, for reasons already discussed, it is not possible of general application. The rebreathing methods aim to obtain either the true venous tensions—that is to say, the tensions of oxygen and carbon dioxide actually occurring in the circulating venous blood—or the "virtual" venous carbon dioxide tension; this is the carbon dioxide tension in the venous blood, which has been oxygenated, but from which no carbon dioxide has been allowed to escape. The former of these involves the production in the subject of a fair degree of artificial asphyxia, and is extremely difficult to apply, requiring the utmost cooperation from the subject and much technical practice in the method by the operator. The "virtual" venous tension method requires the rebreathing of a mixture of carbon dioxide and oxygen for a number of times and is simple to apply; but it has the disadvantage, in common with all methods depending on multiple rebreathings, that there is no certainty as to when equilibrium has been reached between the carbon dioxide in the rebreathing bag and that in the alveoli. To attain this certainty some kind of internal check is desirable.

4. The duration of any rebreathing must not exceed the time of circulation.

5. The arterial and venous levels of carbon dioxide, because of their lability, ideally should be determined together within the one circulation time as pointed out by Bock, Field *et alii*.[23]

6. Whenever possible, a pilot experiment should be performed in order to reassure the subject of the innocuous nature of the procedure.

7. Subjects should not be chosen who have any gross pulmonary lesion likely to cause slowing of the diffusion of carbon dioxide from the capillaries to the alveoli, for this would cause the tension in the alveoli to be appreciably lower than in the blood. This disadvantage would only apply to the alveolar samples, for it would only prolong the time required for and not prevent the attainment of equilibrium by rebreathing.

8. The carbon dioxide dissociation curve should be determined for the blood of each subject investigated.

Experimental Methods.

The problems set out above were considered and a method was developed to solve them. The subjects, ten in number, were males attached to the staff of the medical school of the University of Sydney. With two exceptions they had had no experience at all with the respiratory procedures involved. They presented themselves at the laboratory in the basal state in the morning and rested on a bed for at least forty-five minutes in order that the effects of any physical effort should wear off. The gaseous exchange was then determined by the Douglas bag method. Next the alveolar air samples were taken. The subject still remained on the bed and a nose clip was applied and the rubber mouthpiece of the complex illustrated in Figure V was inserted in the mouth. The tap was turned so that the subject was breathing to the outside air, the rubber bag being in the deflated condition. The only instruction given to the subject was to expire sharply at a given signal. A running one-way conversation was maintained by the operator in order to distract the subject's attention from his breathing. This "waiting" period was timed by stop-watch at three minutes, when, at the end of either an expiration or an inspiration as desired, the tap was turned from the air to the bag B and the subject was told to "breathe out".

The extent and quickness of the response could be judged from the rate at which the rubber bag expanded.

When the expiration was completed a sample was taken first into one gas sampler (S) and immediately afterwards into the other. Because of the valve V, which prevented all respiratory movement but expiration, these samples came from the pulmonary and instrumental dead spaces, which are now filled with air from the alveoli. These samples, owing to the vacuum in the samplers, were actually sucked out under reduced pressure, and in most cases the carbon dioxide content of the second sample was in agreement with that of the first, showing that true alveolar samples had been attained. Several determinations were made at the end of the inspiratory and expiratory phases of respiration and the results were averaged. In later experiments, when the lability of the alveolar carbon dioxide became more apparent, the taking of alveolar samples was combined with the rebreathing procedure, shortly to be described, in order that the calculated arterio-venous difference should relate to blood having the same carbon dioxide level. In those cases in which absolute agreement between the first and second alveolar samples was not obtained the experiment was repeated, with the result that generally this agreement was attained; this fact pointed to the previous disagreements having been due to contamination of the alveolar air with air from elsewhere. In one notable instance, however, in which the subject (M.G.) was an athlete and was technically acquainted with the procedure, agreement between the first and second samples was never attained. Despite repeated experiments, the second sample always yielded a carbon dioxide content higher by a constant amount than the first, nor did it matter which phase of respiration was being examined. In this case, as with the others, the results were averaged.

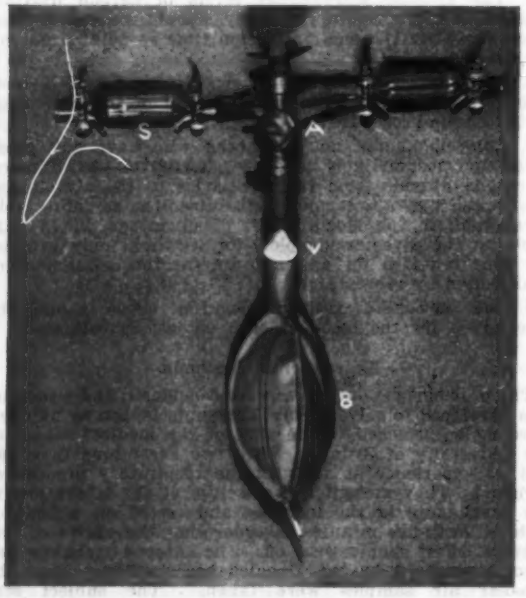

FIGURE V.
Apparatus for obtaining alveolar air samples. A: aluminium tap; V: valve; S: gas samplers; B: rubber bag.

The "virtual" venous carbon dioxide tension was determined by the rebreathing of a mixture of 10% carbon dioxide and 90% oxygen from a rebreathing bag complex similar to that used by Grollman, with the exception that the samples were taken from the distal end of the bag. This was done because, when equilibrium is reached by rebreathing, it is most easily recognized by the presence of complete homogeneity throughout the lung rebreathing bag system; it is immaterial from which phase of respiration or indeed where in the respiratory cycle the samples are taken. After the nose clip had been applied to the subject and a waiting period of three minutes had elapsed, during which period the subject expired to the air, he was instructed to expire deeply and sharply, whereon the tap was turned and the mixture in the bag was breathed back and forth. The volume of this mixture varied between 2·0 and 2·5 litres, and about seven respirations were required in eighteen seconds or less if the subject could manage it. A sample was drawn off from the bag into a sampler at the end of the fifth and again at the end of the seventh respiration. This constituted the experiment, for no multiple rebreathings were required. If equilibrium had been attained, the carbon dioxide content of each sample would be precisely the same; if there had been insufficient time for this to be achieved, then the carbon dioxide content of the first sample would be higher than that of the second, and if there had been any appreciable recirculation, then the content of the second sample would be higher than that of the first. This is illustrated graphically in Figure VI. There is a possible source of

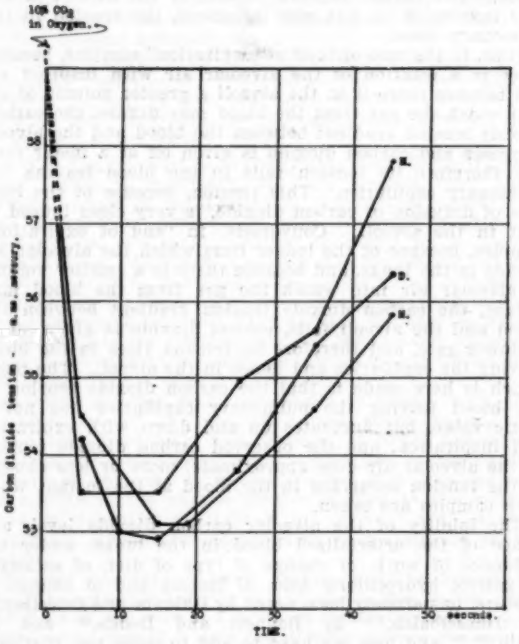

FIGURE VI.
Graph showing the production of plateaux in carbon dioxide tension in the rebreathing bag during the one rebreathing of 10% carbon dioxide in oxygen.

fallacy here, in that such an amount of recirculation may occur by the time the second sample is taken as exactly to offset a lack of equilibrium between the blood in the pulmonary capillaries and the lung rebreathing bag system existing when the first sample was taken; but the probability that this has occurred must be very remote indeed, and it can be made of negligible importance by performing a duplicate experiment and comparing results. An adequate time should be allowed between experiments to permit the washing out of carbon dioxide absorbed and retained during the previous experiment. If the carbon dioxide content of the two successive samples varied appreciably at all, the results were rejected and the experiment was repeated, but such variation was seldom observed.

Unsteadiness of the level of the venous carbon dioxide tension was frequently observed in the same subject on the same morning, and since the oxygen in the rebreathing bag at the end of an experiment was never found to be less than 40%, the possibility that this unsteadiness might be due to a variation in the oxygenation of the blood was

ruled out and the observed lability was considered a true and not a factitious phenomenon. For this reason it was important to determine the arterial and venous carbon dioxide tensions whilst the level in the blood was constant, and the complex shown in Figuure VII was evolved (after Field *et alii*). It consists essentially of a three-way aluminium tap "A.", by means of which the subject can be switched from breathing air to the valve system for taking alveolar samples "S.A.", and from here to the rebreathing bag system "R.B." Unfortunately it was not available for more than two of the subjects investigated; but it gave good results, though it requires a little deftness to take the alveolar samples and to complete the rebreathing within eighteen seconds.

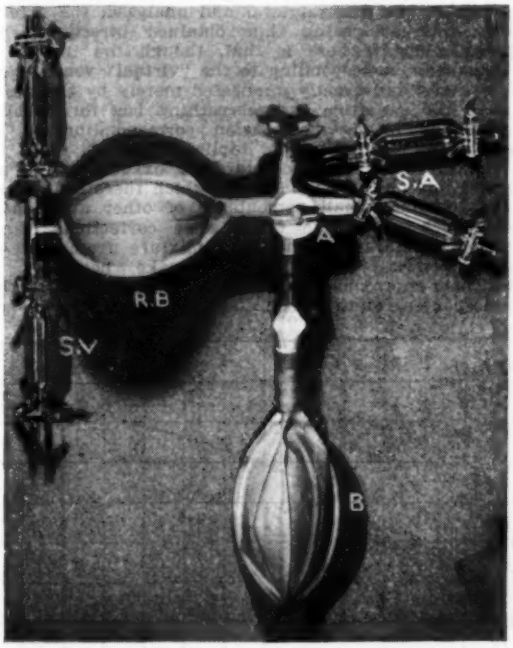

FIGURE VII.

Apparatus for determining the alveolar gas tensions and the "virtual" venous carbon dioxide tension within the one circulation time. A: aluminium three-way tap; S.A.: gas samplers for alveolar air; B: rubber bag for checking volume of alveolar expiration; R.B.: rebreathing bag containing 10% carbon dioxide in oxygen; S.V.: gas samplers for virtual venous carbon dioxide tension.

It was concluded, as set out above, that a true lability exists in the carbon dioxide tension of the venous blood analogous to that postulated for arterial blood. Whether this means that in the resting subject the arterio-venous carbon dioxide difference is also a labile quantity, or that this is a constant and the level of the carbon dioxide tension of the venous and of the arterial blood rises and falls in unison, I was not able to decide experimentally, for it is evident that the two last-mentioned values must be determined as nearly simultaneously as possible before any opinion can be advanced about the former possibility. A fluctuant arterio-venous difference does not necessarily mean a fluctuant cardiac output provided the gaseous exchange varies also in direct proportion. However, the opinion is held that, though the level of the carbon dioxide tensions in the blood may vary, the arterio-venous difference is relatively constant.

Pilot experiments were performed in only five instances, because the subjects could ill afford the time, and in any case, since they were acquainted with the laboratory and the operator, it was considered that there was less likelihood of their being disturbed by the procedure than if they were strangers. However, even in these circumstances a pilot experiment on all subjects would have been a desirable refinement.

The carbon dioxide dissociation curve in fully oxygenated blood was determined for each subject. Figure IV shows six of these curves; the others are not reproduced, because they almost duplicate existing curves. It can be seen that there is some diversity in shape and position amongst the curves. These curves were obtained in the following way:

About 10 cubic centimetres of blood were taken without stasis from the antecubital vein into anticoagulant and fluoride, the latter being to prevent glycolysis. The blood was then transferred to a large tonometer of about 400 cubic centimetres' capacity, which was clamped in the upright position. Carbon dioxide (about 3%) in oxygen was bubbled through the blood, which frothed, and as the froth rose it displaced the air from the tonometer and at the same time presented a large surface to the gas mixture, thus facilitating the attainment of equilibrium. This is illustrated in Figure VIII. The tonometer was then transferred

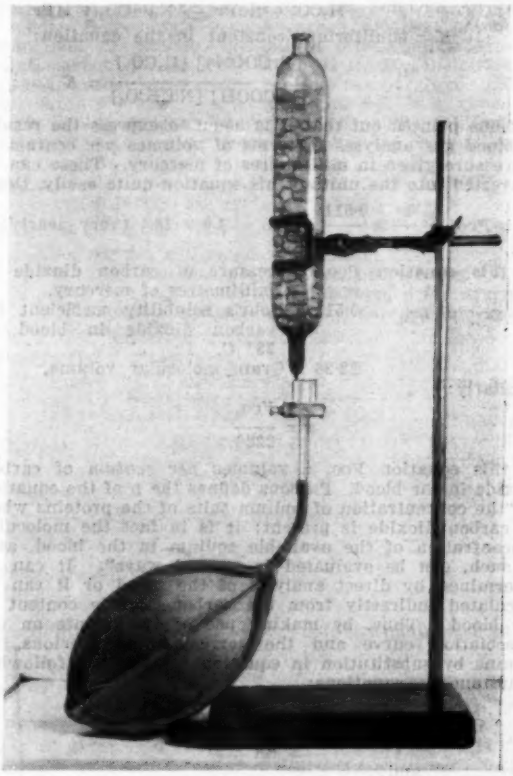

FIGURE VIII.

Method of displacing air over blood in tonometer with gas mixture of known composition. As the gas is passed in the blood froths, carrying up with it the contaminating air and at the same time it displays a greatly increased surface to the incoming gas, thereby facilitating the attainment of equilibrium.

to a water bath at 37° C.; the pressure was adjusted and equilibrated by rotation for fifteen minutes. Blood samples (one cubic centimetre) were analysed in duplicate by Van Slyke's method in the manometric apparatus for carbon dioxide content, the result being expressed in volumes *per centum*. The gas from over the blood in the tonometer was also analysed for carbon dioxide content, the result being expressed in millimetres of mercury.

The whole experiment, the remainder of the blood from this equilibration being used, was repeated with a higher concentration of carbon dioxide (about 10%) in oxygen.

The carbon dioxide content, together with the corresponding tensions, were thus determined for two points on the dissociation curve for fully oxygenated blood, and these were applied to the solution of Parsons's equation, now to be discussed.

Discussion.

Parsons[(20)] applied the law of mass action to the state of carbon dioxide in the blood and derived the following equation:

$$x = \frac{-y + \sqrt{y^2 + 4Kyp}}{2K} \quad .. \quad .. \quad (i)$$

in which x = molecular concentration of combined carbon dioxide.

y = molecular concentration of free carbonic acid.

p = molecular concentration of the sodium proteinate when the carbon dioxide tension approaches zero in the equation:

$$H_2CO_3 + NaPr \rightleftarrows NaHCO_3 + HPr.$$

K = equilibrium constant in the equation:

$$\frac{[PrCOONa]\,[H_2CO_3]}{[PrCOOH]\,[NaHCO_3]} = K$$

Parsons pointed out that it is usual to express the results of blood gas analyses in terms of volumes *per centum* at a pressure given in millimetres of mercury. These can be converted into the units of his equation quite easily, thus:

$$y = P_{CO_2} \times \frac{1}{760} \times \frac{0{\cdot}511}{22{\cdot}26} = P_{CO_2} \times 3{\cdot}0 \times 10^{-5} \text{ (very nearly)}$$

In this equation P_{CO_2} = pressure of carbon dioxide in millimetres of mercury.

0·511 = Bohr's solubility coefficient for carbon dioxide in blood at 38° C.

22·26 = Gram molecular volume.

Similarly:

$$x = \frac{V_{CO_2}}{2226}$$

In this equation V_{CO_2} = volumes *per centum* of carbon dioxide in the blood. Parsons defines the p of the equation as "the concentration of sodium salts of the proteins when no carbon dioxide is present; it is in fact the molecular concentration of the available sodium in the blood, and, as such, can be evaluated in several ways". It can be determined by direct analysis of the blood or it can be calculated indirectly from the carbon dioxide content of the blood. Thus, by making use of two points on the dissociation curve and the corresponding tensions, he obtains by substitution in equation (i) the two following simultaneous equations:

$$x_1 = \frac{-y_1 + \sqrt{y_1^2 + 4Ky_1p}}{2K}$$

and

$$x_2 = \frac{-y_2 + \sqrt{y_2^2 + 4Ky_2p}}{2K}$$

from which by simplification he derives the following:

$$K = \frac{(y_1y_2) \times (x_1 - x_2)}{(x_2^2y_1) - (x_1^2y_2)} \quad .. \quad .. \quad (ii)$$

$$P = \frac{x_2 + Kx_2^2}{y_2} \quad .. \quad .. \quad .. \quad .. \quad (iii)$$

Thus, with no more data than those obtained from carbon dioxide analyses of blood equilibrated at two different tensions and the derivation of K and p from these values and their subsequent substitution, together with the values corresponding to any desired tension, the carbon dioxide content of the blood at this tension can be calculated. If a number of varying tensions are taken, the position and shape of the dissociation curve can be determined. This curve, as shown by Parsons, from whose paper Figure IX is taken, duplicates that determined by direct analysis of the blood. In the determination of the arterio-venous difference it is not necessary to reproduce the dissociation curve *in toto*, or indeed at all, for the carbon dioxide content of the blood corresponding to the arterial and virtual venous tensions is all that is required. Since, in effect, the carbon dioxide content of the venous blood is determined by recourse to the curve for fully oxygenated blood, the importance of maintaining a high tension of oxygen in the rebreathing bag can be seen. Parsons's equation need not be used, but the blood can be equilibrated with carbon dioxide in oxygen corresponding to the "virtual" venous level and to the arterial level and analysed, the arterio-venous difference being thus obtained directly. The technical difficulty here is that, though the tension in the tonometer corresponding to the "virtual" venous level can be easily and exactly duplicated merely by the use of some of the gas from the rebreathing bag for bubbling through the blood, the tension corresponding to the arterial level is difficult to duplicate exactly, since the gas mixture must be made up from oxygen and carbon dioxide contained in cylinders, in which there are present as contaminants small percentages of other atmospheric gases which necessitate troublesome corrections. Any variation whatever in the final mixture from the calculated arterial tension would make necessary an undesirable approximation in the computing of the carbon dioxide content of the blood.

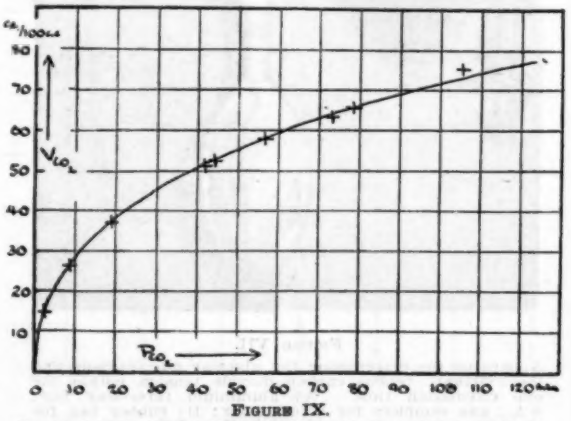

FIGURE IX.

Comparison between theoretical curve, derived by Parsons, and the experimental results for fully oxygenated blood, of Haldane. (From Parsons, *The Journal of Physiology*, Volume LIII, 1919.)

The derivation of the values for K and p and their substitution are not difficult at all, as can be seen from the following example (Table III; subject A.K.M.).

TABLE III.

Analysis of Equilibrated Blood.

Carbon Dioxide. Volume Percentage.	Carbon Dioxide. Tension in Millimetres of Mercury.
42·3	27·6
55·3	59·3

$$K = \frac{y_1y_2(x_1 - x_2)}{x_2^2y_1 - x_1^2y_2}$$

Now $y = P_{CO_2} \times 3 \times 10^{-5}$

$y_1 = 27{\cdot}6 \times 3 \times 10^{-5} = 8{\cdot}28 \times 10^{-4}$

$y_2 = 59{\cdot}3 \times 3 \times 10^{-5} = 17{\cdot}79 \times 10^{-4}$

Now $x = \frac{V\text{co}_2}{2226}$

$$x_1 = \frac{42{\cdot}4}{2226} = 1{\cdot}900 \times 10^{-2}$$

$$x_2 = \frac{55{\cdot}3}{2226} = 2{\cdot}485 \times 10^{-2}$$

By substitution:

$$K = \frac{(8{\cdot}28 \times 17{\cdot}79 \times 10^{-6})(1{\cdot}9 - 2{\cdot}485) \times 10^{-2}}{[(2{\cdot}485 \times 10^{-2})^2 \times (8{\cdot}28 \times 10^{-4})] - [(1{\cdot}9 \times 10^{-2})^2 \times (17{\cdot}79 \times 10^{-4})]}$$

which simplifies to

$$K = 6{\cdot}582 \times 10^{-3}$$

$$p = x_2 + \frac{Kx_2^2}{y_2} \quad \text{or} \quad x_1 + \frac{Kx_1^2}{y_1}$$

By substitution:

$$p = 1{\cdot}900 \times 10^{-2} + \frac{6{\cdot}582 \times 10^{-3} \times 3{\cdot}61 \times 10^{-4}}{8{\cdot}28 \times 10^{-4}}$$

which simplifies to

$$p = 4{\cdot}769 \times 10^{-2}$$

Again:

$$x = \frac{-y + \sqrt{y^2 + 4Kyp}}{2K}$$

Let $P\text{co}_2 = 10$ millimetres.

Then $y_{10} = 3 \times 10^{-4}$

$$x_{10} = \frac{-3 \times 10^{-4} + \sqrt{9 \times 10^{-8} + 376{\cdot}68 \times 10^{-8}}}{13{\cdot}164 \times 10^{-2}}$$

$$= \frac{-3 \times 10^{-4} + \sqrt{385{\cdot}68 \times 10^{-8}}}{13{\cdot}164 \times 10^{-2}}$$

$$= \frac{-0{\cdot}03 + 0{\cdot}1963}{13{\cdot}164}$$

$(V\text{co}_2 = x_{10} \times 2226)$

Therefore $V\text{co}_2 = \frac{0{\cdot}1663}{13{\cdot}164} \times 2226$

$= 28{\cdot}1$ volumes *per centum*.

The accompanying table (Table IV) shows the results obtained from ten normal subjects. The cardiac output varies from 3·2 to 4·4 litres per minute and the cardiac index from 1·9 to 2·4 litres per square metre per minute, the mean value being 2·1. The alveolar carbon dioxide tension was determined at least twice at the end of each respiratory phase and the results were averaged. The mean of the "inspiratory" and "expiratory" samples was taken as representing the average carbon dioxide tension in the alveoli and hence in the arterialized blood in the lungs. Lability of the "virtual" venous and of the alveolar carbon dioxide tension was observed in most subjects—indeed in one, A.H., it was such that the average of "end of inspiration" samples was more than the average of "end of expiration" samples. It was in order to avoid this possible source of fallacy that the complex illustrated in Figure VII, following the arrangement used by Field *et alii*, was evolved. By its use the "virtual" venous and the alveolar carbon dioxide tensions can be determined within the one circulation time. The alveolar carbon dioxide tension was determined during the time the subject was breathing air, and therefore with the blood 95% saturated with oxygen. The observed alveolar carbon dioxide tensions are therefore slightly lower and the arterio-venous difference is slightly higher than would have been the case had pure oxygen been breathed; but this discrepancy is likely to be insignificant. However, some tentative experiments seem to show that there is better agreement between each pair of samples when pure oxygen is breathed. Table IV also shows great variation in the carbon dioxide content of the arterial and venous blood of the ten subjects, in some of whom, indeed, the venous carbon dioxide content is lower than the arterial content of others. The arterio-venous carbon dioxide difference was fairly constant with the mean value of 43 cubic centimetres per litre, and if the respiratory quotient is taken as 0·8, this gives an arterio-venous oxygen difference of 54 cubic centimetres per litre, as can be seen from the following calculation:

$$C.O. = \frac{O_2}{A.V.D.(O_2)} \quad \text{or} \quad \frac{CO_2}{A.V.D.(CO_2)} \quad \ldots \ldots \quad (1)$$

where $C.O.$ = cardiac output,

O_2 = oxygen consumed per minute,

CO_2 = carbon dioxide produced per minute,

$A.V.D.\ (O_2)$ = arterio-venous difference for oxygen,

$A.V.D.\ (CO_2)$ = arterio-venous difference for carbon dioxide.

From (1):

$$\frac{CO_2}{A.V.D.\ (CO_2)} = \frac{O_2}{A.V.D.\ (O_2)}$$

That is:

$$\frac{CO_2}{O_2} = \frac{A.V.D.(CO_2)}{A.V.D.(O_2)}$$

But $\frac{CO_2}{O_2} = R.Q. = 0{\cdot}8$ by hypothesis.

Therefore $0{\cdot}8 = \frac{43}{A.V.D.(O_2)}$

Therefore $A.V.D.(O_2) = \frac{43}{0{\cdot}8} = 54$ cubic centimetres per litre.

TABLE IV.

Subject.	Age. (Years.)	Surface Area. (Square Metres.)	Pulse Rate per Minute.	Respirations per Minute.	Alveolar CO_2. Inspiratory.[1]	Alveolar CO_2. Expiratory.[1]	Alveolar CO_2. Mean.[1]	"Virtual" Venous CO_2 Tension.[2]	Blood. Arterial CO_2 Tension.[2]	Blood. Venous CO_2 Tension.[2]	Arterio-venous CO_2 Difference. (Cubic Centimetres per Litre.)	CO_2 Production per Minute. (Cubic Centimetres.)	Cardiac Output. (Litres per Minute.)	Cardiac Index. (Litres per Square Metre per Minute.)	Stroke Volume. (Cubic Centimetres.)
K.C. ..	20–25	1·8	75	16	43·7	46·2	45·0	52·9	54·3	58·3	40	166	4·2	2·3	56
M.M. ..	30–35	1·8	63	14	40·0	40·2	40·1	51·9	52·7	56·7	40	166	4·2	2·3	67
W.J.L. ..	35–40	1·94	62	14	39·1	43·8	41·5	51·5	49·6	53·9	43	172	4·0	2·1	65
M.G. ..	25–30	1·9	60	14	40·2	42·4	41·1	50·0	48·5	52·6	41	150	3·7	1·9	63
A.K.M. ..	25–30	1·7	60	12	43·5	44·0	43·75	55·0	49·8	53·9	41	161	3·9	2·3	65
J.P.S. ..	25–30	1·63	68	15	45·8	46·0	45·9	53·3	49·0	52·6	36	114	3·2	2·0	47
R.B. ..	25–30	1·84	65	24	39·4	44·6	42·0	51·8	50·0	54·2	42	151	3·6	2·0	55
A.H.[1] ..	20–25	1·58	62	—	45·9	44·9	45·4	57·1	50·0	54·4	44	146	3·3	2·1	53
S.W.S. ..	35–40	2·1	70	15	38·6	39·2	38·9	49·8	45·7	51·1	54	239	4·4	2·1	63
J.S. ..	20–25	2·0	63	12	38·1	42·6	40·4	51·9	49·1	53·8	47	227	4·8	2·4	76
Mean ..	—	1·83	—	—	41·4	43·4	42·4	52·5	49·8	54·1	43	—	3·9	2·1	61

[1] Alveolar expiratory carbon dioxide tension is less than the inspiratory tension, probably owing to change in the arterial carbon dioxide level during the experiment.

[2] Millimetres of mercury. [3] Volumes *per centum*.

It can be seen from Table IV that if there is a corresponding diminution in the carbon dioxide production, a low arterio-venous difference does not necessarily result in a high cardiac output, and *vice versa*.

It is of the utmost importance that the carbon dioxide output shall be determined accurately, and in order to guard against "washing out" by overbreathing and similar errors inseparable from experiments on respiratory exchange, it is desirable to repeat this part of the procedure several times with the usual precautions, and at the same time to extend it to involve the determination of the basal metabolic rate. When this value has settled down, the value for carbon dioxide output can be accepted with confidence. The determination of the respiratory exchange can never be coincident with the determination of the arterial and venous carbon dioxide levels, but must be antecedent or subsequent thereto. It follows that if for any reason, such as simple overbreathing, Cheyne-Stokes breathing or change in metabolic state, there is a variable carbon dioxide output from time to time, it may be related to an arterio-venous difference determined at a time when, in point of fact, the respiratory exchange was different, and this would result in a false value for cardiac output. Suppose, for example, the arterio-venous difference to be 40 cubic centimetres per litre and the carbon dioxide output 160 cubic centimetres per minute; then the calculated cardiac output is 4·0 litres per minute. Now suppose that the carbon dioxide output has varied by 10% (in reality not a considerable amount) and becomes 176 cubic centimetres per minute; then the cardiac output computed from the same arterio-venous difference increases in direct proportion and becomes 4·4 litres per minute. On the other hand, any change in the arterio-venous difference causes an inversely proportional change in the cardiac output.

The variations, shown in Table IV, of the cardiac index from the generally accepted value of 2·2 litres per square metre per minute are quite small, and are probably due to a combination of the factors mentioned above, the chief of which are lability of the carbon dioxide levels in the arterial and venous blood, variation in metabolic state, and variation in carbon dioxide output. The technique is capable of further refinement in regard to the determination of the arterial carbon dioxide content.

Summary.

A review has been made of the technical difficulties in the application of the carbon dioxide method for the determination of the cardiac output.

A simple method has been described for the determination, during one rebreathing only, of the "virtual" venous carbon dioxide tension. A refinement in the technique for obtaining alveolar air is also described.

Evidence has been adduced of the lability of both the venous and the arterial carbon dioxide levels, and the desirability is stressed of determining these values as nearly simultaneously as possible.

The desirability of producing a dissociation curve for the blood of each subject is pointed out and the importance and usefulness of Parsons's work in this regard is shown.

The importance, in regard to the calculation of the cardiac output, of the precise determination of the respiratory exchange is commented on, and attention is drawn to the fact that the arterio-venous oxygen difference can be simply and accurately calculated from the arterio-venous carbon dioxide difference.

It is suggested that there should be at least one pilot experiment in order to accustom the subject to the procedure.

The advantage of extending the procedure so as to involve the determination of the basal metabolic rate as a further check is also suggested.

Acknowledgements.

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Reports of Cases.

PLASTIC RECONSTRUCTION OF THE CHEEK AFTER AN EXTENSIVE EPITHELIOMA.

By RICHARD FLYNN,
Sydney.

Clinical Record.

J. B. McM., a male patient, aged forty-one years, was admitted to the Royal Prince Alfred Hospital on June 28, 1933, suffering from a large epithelioma of his right cheek. His history was that one and a half years previously he had noticed a small lump in his right cheek, which had gradually enlarged and ulcerated. He was given X-ray therapy at another hospital, and later (ten months ago) he was admitted to that institution and radium needles were

FIGURE I.

inserted. After this treatment the lump disappeared until five months before his admission to hospital, when he noticed a hard lump in the site of the original lump, which increased rapidly in size. Six weeks previously he also had noticed a swelling just beneath his jaw on the right side of his neck, and this also increased rapidly in size. On this occasion he was treated by implantation of radium needles, and a total dose of 5,000 milligramme-hours was given.

On October 5, 1933, a radical dissection of the glands of the right side of his neck was performed. The pathological report on the excised tissue was as follows:

Macroscopic. The tissue from the neck includes a large spherical mass which measures 3·5 cm. in longest diameter. The cut surface of this is smooth and white, but in places there is a faint suggestion of a grain.

Microscopic. The cells of the tumor are mainly spindle shaped and they are arranged in a fasciculated manner. In many areas there are large cells which have large irregular nuclei. There are numerous cells with degenerated and deeply eosinophilic cytoplasm which suggests that the tumor may be a spindle celled epithelioma.

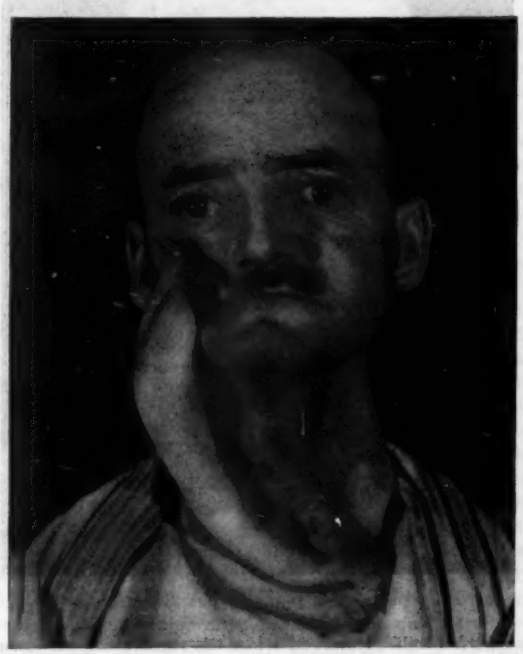

FIGURE II.

On October 2, 1934, he was readmitted to hospital, and on examination he was found to have a large ulcerated area on the right side of his face. It extended from the angle of the mouth anteriorly to about the anterior border of the masseter muscle posteriorly, and from just below the zygomatic arch superiorly to the alveolar margin of the mandible inferiorly. The continuity of the cheek was not broken, but he had a large ulcer at the corresponding site on the mucous surface of his cheek. At that time I was not familiar with Patterson's work on securing homogeneous dosage through a large carcinoma by the "sandwich application" of radium, so owing to the unsatisfactory response to the radium treatment used, the involved area of the cheek and the outer wall of the maxilla were removed by the diathermy knife on October 14, 1934. The pathological report by Dr. G. F. S. Davies on sections of this tissue removed was as follows:

> The sections have been compared with those from a previous biopsy. These were reported on as spindle cell epithelioma. The cells are large, elongated and tend to form into clumps or strands. In the first biopsy the cells are large and more regular, but are very much elongated and in many ways resemble smooth muscle cells. Numerous sections have been examined and it has been found impossible to discover any transition between these cells and more typical epithelial cells. If the growth is an epithelioma it is an extremely atypical one and it is difficult to say how its origin can be proved.

On November 1, 1934, a radical dissection of the glands of the left side of the neck was performed. Microscopic examination failed to reveal any evidence of the involvement of lymphatic glands with carcinomatous metastases.

After healing of the edges of the wound in his face (Figure I) the patient was fitted with a dental prosthesis in an attempt to make him appear less unsightly; but he preferred to wear a gauze dressing to cover his deformity. After a waiting period of approximately two years a beginning was made to reconstruct his face. Two tube grafts were raised from the skin of the anterior surface of his chest in September, 1936. The intention at that time was to use one tube for the replacement of the external half of the lost tissue and the other for the replacement of

FIGURE III

its internal half. However, when the right graft was swung up to his face a considerable portion of the tube became gangrenous and was lost. The portion of the tube which remained vital was sewn to the cut distal end of the left tube, after the method of Gillies, and after a suitable period of delay (about one month), during which the proximal end of the right graft was tied off for increasing periods, the right end of the sling so formed was divided, swung up and attached to the right masseter region (lower and posterior border of the hole) (Figure II). A month later the attached end of the original left tube was divided and sewn onto the right free end of the upper lip. Once the lengthy tube was attached to the face at both ends it was an easy matter to arrange portions to fill in the cheek (Figure III). As will be noticed from the photographs, there is a large amount of fat in the flaps; the patient gained over two stone in weight while these flaps were being fashioned and transplanted. The fat was removed from the graft, and it will be noticed from a comparison of Figures III and IV how well the flap above the angle of the mouth has settled down. But though fat has been removed from the lower area on three separate occasions, it still looks too bulky. However, I feel that this thickening is due more to a chronic œdema than to fat (Figure IV). I had thought at one time to help give support to the newly formed cheek with *fascia lata* strips; but as the patient is satisfied, and as the procedure is not without risk to his newly formed cheek, I have advised him against it. To overcome the drag on the lower eyelid and the subsequent exposure of the globe an "Esser graft" was inserted in the cheek just beneath the orbital margin.

Comment.

The case is interesting for the following reasons:

1. The cure of an extensive carcinoma of the face is demonstrated. A cure can be claimed, as there is no sign of recurrence and it is now over seven years since the patient's lesion was excised.
2. A method of replacing an extreme amount of lost substance has been evolved so as to enable a healthy adult to resume his economic position.
3. Reconstruction of the face, when neck sites for tube grafts were not available owing to extensive bilateral dissection of the glands of the neck, has been demonstrated.
4. The internal surface of the flaps now has the appearance of normal mucous membrane.

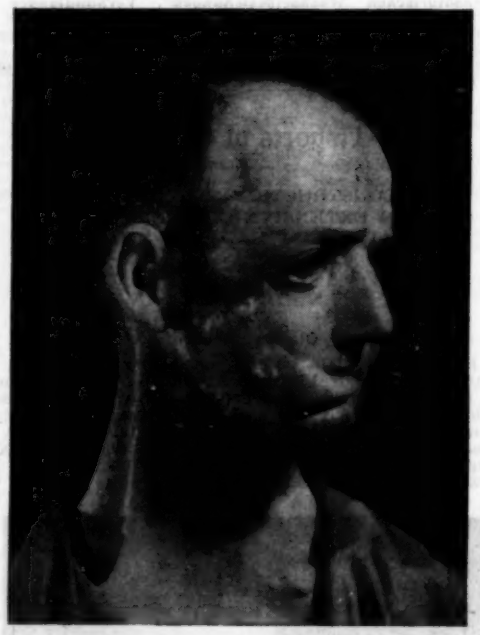

FIGURE IV.

Acknowledgement.

My thanks are due to Mr. Woodward Smith, of the medical artistry department of the University of Sydney, for the photographs that illustrate this case report.

Notes on Books, Current Journals and New Appliances.

DISORDERS OF BLOOD PRESSURE.

ANOTHER of "The Practitioner" booklets has been issued. This, the fifth volume, deals with disorders of blood pressure,[1] and *The Practitioner* is to be congratulated thereon. From time to time articles on blood pressure have appeared in *The Practitioner*, and those recently published form the basis of the present booklet. The chapters are six in number. G. W. Pickering opens with a discussion on the significance of high blood pressure and its complications. K. Shirley Smith writes on the measurement of arterial blood pressure and makes special reference to life assurance examinations. John Hay deals with the treatment of patients with high blood pressure, Douglas McAlpine with the cerebral manifestations of arterial disease, W. W. D. Thomson with nephrosclerosis and malignant hypertension, and H. J. Starling with hypotension. As the editors write in the preface, the ultimate effects of raised blood pressure upon the heart, the brain and the kidneys form a large chapter in modern medicine. Those who read this booklet will be helped by it. It is a pity that it cannot be sold in Australia at its English price.

[1] "Disorders of Blood Pressure", by various authors, edited by Sir H. Rolleston, Bt., G.C.V.O., K.C.B., M.C., F.R.C.P., and A. Moncrieff, M.C., F.R.C.P.; 1942. London: Eyre and Spottiswoode Limited. Medium 8vo, pp. 93, with 9 illustrations. Price: 6s. net.

The Medical Journal of Australia

SATURDAY, MAY 9, 1942.

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MINOR VITAMIN DEFICIENCIES.

IT is one thing to have text-book knowledge of a subject; it is another to apply that knowledge wisely in the treatment of a sick patient. This is true of vitamins and vitamin deficiencies as of any other subject in medicine. Any general practitioner could in all probability produce at a moment's notice quite a useful account of the several vitamins and of the symptoms likely to follow their exclusion from the diet. If he found difficulty in regard to nomenclature or any other point he could readily refresh his memory from one of the many tabulations issued from time to time by enterprising drug manufacturers. Whether he could obtain satisfactory results without delay in the treatment of a patient suffering from vitamin deprivation would depend on several factors. The first and most important of these factors would be the extent to which the patient was affected—whether the condition was one of the well-known stereotyped entities such as rickets, beriberi, pellagra or scurvy. If the condition was one of these obvious entities the task would in nine cases out of ten be simple, the chief difficulty probably being that of making the patient do as he was told. But in Australia, if not in other countries, the condition is seldom clear cut and obvious—severe vitamin deprivation is not common—and it is, moreover, true that if one vitamin is lacking from the diet, the others are not likely to be present in their right amounts. Both these facts complicate diagnosis even if they do not make the treatment more difficult once a diagnosis has been made. Of course, vitamin deficiency may be an accompaniment or a predisposing factor of any illness caused by an infective or other agent. This probably happens much oftener than is suspected, and under present war conditions, when some foods are unobtainable and others are so expensive that people with ordinary means cannot afford to buy them, should be kept constantly in the mind of the clinician.

At the annual meeting of the American Medical Association last June, J. M. Ruffin read a paper before the Section on Pharmacology and Therapeutics on the diagnosis and treatment of mild vitamin deficiencies.[1] Some of his remarks were so timely that attention should be drawn to them. He said that for every patient with an advanced vitamin deficiency there were many with a subclinical or mild deficiency state. He was concerned particularly with this group, and his first care was diagnosis. He referred to the difficulty of the recognition of mild or early vitamin deficiency. Perhaps it may be well to point out that it would be impossible to recognize a subclinical deficiency in any other way than by estimating the vitamin content of the food. The word subclinical has reference to a period prior to the appearance of manifest symptoms in the evolution of a disease; some clinicians use the word without appreciating its real significance. The point is important and not a quibble about words. Ruffin illustrates this. He states that improvement after vitamin therapy in such symptoms as flatulence, indigestion, weakness, nervousness and irritability does not necessarily constitute proof of a deficiency state. Improvement in such a vague clinical picture should, he adds, be construed only as suggestive evidence of a state of subclinical deficiency. If such symptoms are evidence of such a state, they are the symptoms of the state and the condition is not subclinical. Though we may not agree with Ruffin about the use of words we can accept his suggestion that deficiency in the diet may be responsible for mild symptoms; and these obviously may become severe if the deficiency is long continued or becomes greater. The early symptoms of a vitamin deficiency are important. Among them are many which are typical of the so-called gastric neuroses, psychoneuroses and neurasthenia. Clearly it may be impossible to prove whether a vitamin deficiency is responsible. Further, even if there are strong grounds for suspicion that vitamin deficiency is the *fons et origo mali*, it may be no simple matter to determine which of the vitamins is concerned. The chances are, as Ruffin states, that the signs indicate a mixed deficiency; as already indicated, simple deficiencies rarely if ever occur spontaneously. The position must be that taken up by Ruffin—that patients presenting early symptoms of a vitamin deficiency must be merely suspected of suffering from such a condition, a definite diagnosis being made only after positive evidence has been obtained. What then are the manifestations, what positive evidence is necessary before a positive diagnosis can be made? As already pointed out, the advanced stages of vitamin deficiencies have typical clinical pictures which point to a diagnosis. But during the development of this state of deficiency certain conditions appear which justify the diagnosis. There are certain laboratory procedures which may be of assistance, but, as Ruffin reminds us, most of them require special apparatus and well-trained technicians. There is no need to enumerate the symptoms associated with different kinds of deficiency since we are at the moment concerned more with broad principles than with details. But in regard to laboratory procedures it is true that the determinations of the blood level of vitamin *C* and of the prothrombin time can be carried out in any well-equipped laboratory; the demonstration, however, of a deficiency in vitamin *A*, in nicotinic acid, in vitamin B_1 or in riboflavine are in the province of the special investigator. Thus we come to the conclusion that in general practice the diagnosis of vitamin

[1] *The Journal of the American Medical Association*, November 1, 1941.

deficiency will depend largely "on a proper evaluation of the symptoms and signs . . . and their response to therapy".

The practitioner thus has thrust upon him a grave responsibility—on the one hand he must be watchful lest he overlook a vitamin deficiency whose symptoms cry out for recognition either alone or in association with some other pathological condition; on the other hand he has to guard against too much zeal, having which he would see deficiencies over and over again where none existed. Failure in either case would probably lead to therapeutic disaster. The general public has learned a great deal about vitamins and is prepared to be taught that the proper treatment of vitamin deficiencies is their prevention. Popular knowledge is useful, but it carries with it the danger that a diagnosis of vitamin deficiency may become the fashion. There are fashions in diagnoses just as there are in drugs and in women's clothes, though, we should be thankful, not to the same extent. It may be argued that no harm will be done if a vitamin deficiency is diagnosed where none exists, even if the creation or perpetration of a fashion is encouraged. It may also be said that vitamin therapy in many cases can be regarded as a diagnostic test. This is all very well, but the patient must not be told that he is suffering from the effects of a vitamin deficiency unless one has been proved to exist. This is especially necessary if a genuine therapeutic diagnostic test is being carried out, for it may be extraordinarily difficult to exclude the psychological effect of a change in diet that has been carefully explained to the patient beforehand. In any case it will surely be agreed that in vitamin therapy, as in any other branch of therapeutics, shot-gun methods and empiricism should as far as possible be avoided. The subject of vitamins and vitamin therapy is one into which confused thinking and haphazard practice are liable to creep; it is as a warning against these that the present discussion has been undertaken.

Current Comment.

LIMITS OF ELECTROCARDIOGRAPHY.

IT is the fate of every new diagnostic method to be received with hesitancy at first, then to be applied with uncritical enthusiasm, and finally to stand the test of a severe reaction, from which it emerges with its capacities properly delimited. Immense harm can be done by a grave prognosis based on the improper use of a new technique, and this is especially true of cardiac conditions. How many happy beings have been cast into shadow through the detection of a heart murmur by the stethoscope when the circulation was adequate for all ordinary purposes—insurance was refused or heavily loaded and the expectation of sudden death haunted the unfortunate victim often for many years? The latest diagnostic method to enter the period of reaction and criticism is the electrocardiogram, concerning which warnings have come from several quarters of late. It has been pointed out that variations in conduction occur in the same person and in good health; that diagnoses based on the *T* wave are mostly unjustified, and further, that dangerous cardiac conditions, such as angina, may display a perfectly normal electrocardiogram. H. M. Marvin, of Yale, in the February 5 issue of *The New England Journal of Medicine*, has sounded a timely warning against the abuse of the electrocardiogram. According to him, numbers of normal, healthy subjects have been condemned to lives of semi-invalidism on the evidence given by the electrocardiograph in the hands of untrained practitioners, and mention is made that there is a widespread desire amongst American cardiologists for the foundation of a board which would register those competent to use the instrument and interpret its records. It is freely admitted by the most critical that there are conditions on which the electrocardiogram is capable of throwing valuable light. In the arrhythmias, in the involvement of the heart in systemic diseases, such as rheumatic fever and diphtheria, and in acute myocardial infarction the electrocardiograph is without a rival. It can also perform a notable service by assuring those who have become apprehensive about their hearts that nothing abnormal can be detected, and such patients generally accept the negative evidence with satisfaction and relief. Occasions on which grave errors in diagnosis have been committed have been concerned with conduction intervals and especially with ventricular complexes. Further, the information supposed to be given on the functional state of the heart is in some cases absent and in some erroneous. Whilst the early phases of digitalis poisoning can often be first detected electrically, it is a mistake, according to Marvin, to use the electrocardiogram as a guide to the administration of this powerful drug. The experienced physician will certainly agree with the view emphasized by this author that in cardiac diagnosis and prognosis clinical findings should come first and should never be omitted or relegated to a secondary position or be eclipsed.

In the February number of *The American Journal of the Medical Sciences* A. J. Geiger, M. Calabresi and L. F. Blaney, also of Yale, pleaded for an extended use of electrocardiography in hospital practice. This might at first sight be regarded as running counter to Marvin's warning, but the conclusions are guarded. These authors feel that the electric records can be a valuable addition to other findings and that "a full appraisal of the cardiac status is not complete without this adjunct to supplement the history, physical examination, functional tests and roentgenographic study". The uncertainty of the significance of *T* wave abnormalities is admitted. "We are not prepared, therefore, to recommend electrocardiography as a routine examination"; but they suggest that when the heart is obviously pathological or is likely to be involved in certain system diseases, the enlistment of this instrument should not be omitted.

"T.N.T."

"THE internal combustion engine and the high explosive tri-nitro-toluene, belong to the category of doubtful benefits which scientific progress has given the world." This is the opening sentence of an editorial in *The Lancet* of November 15, 1941, in which the question of T.N.T. poisoning is discussed. The stability and low toxicity of this explosive led to little trouble during its peace-time manufacture, but the urgent demand for enormous quantities in war has meant in this war, as in the last, a less careful handling and less perfect supervision of the health of the employees engaged in its manufacture. After the good work of Legge, Moore and others in the 1914-1918 war, who showed that T.N.T. made its way into the body more often through the skin than the alimentary or respiratory passages, and who suggested preventive measures which saved the lives of hundreds of workers in 1917-18, it would have been thought unlikely that many fresh instances of liver damage would ever occur again. Webster's urine test proved of great value in the assessment of the value of various preventions, and revealed the individual differences in absorption of the compound by workers in explosive factories. It appeared reasonable to suppose that ingestion of adequate amounts of vitamin *C* might have played a part in determining the occurrence of such individual differences.

In the last war, toxic jaundice was made a notifiable disease in Great Britain after 1915. This does not appear to be still the case in 1941. The measures taken so successfully in the Great War to prevent the accumulation and absorption of dust and fume are still being applied,

and such has been the advance in the engineering control of industrial risks that we can be sure that they are more efficient than before. Some newly born factories and annexes may be less well equipped and supervised, and wherever human cooperation is required to complete the scheme, errors and omissions can arise. In urging the need for selection of workers, one authority has said that those who are susceptible to T.N.T. may not be protected by even the most satisfactory working conditions and most careful supervision. While it is impossible to determine this susceptibility with any degree of certainty beforehand, there appears to be good ground for rejecting candidates for employment who are very young, very thin and who have very moist hands or a history of jaundice or liver trouble. Short hours in workrooms, adequate ventilation, personal cleanliness, especially of hands and nails, are indispensable, while a full diet unspoiled by food rationing is a necessity.

Reviewing seven cases of T.N.T. jaundice, two of which proved fatal, Robert Evans states[1] that if no toxic phenomena appear within seven months, most workers by then become immune. The symptoms he observed were jaundice, nausea, anorexia and epigastric discomfort. Liver enlargement and pyrexia were absent, distinguishing the condition from catarrhal jaundice, with which it is likely to become confused. Autopsy in the fatal cases revealed acute yellow atrophy of the liver, and hyperplasia of the bone marrow in one case, and subacute liver necrosis and a hyperplastic bone marrow in another, in which death was due to aplastic anæmia. Treatment was by glucose, insulin and vitamin *C*. Ingham has improved the Webster test for the determination of T.N.T. derivatives in the urine. Application of the test regularly to large numbers of workers should prove simple and rapid. By this means, combined with methods such as the quantitative estimation of blood bilirubin, the hippuric acid test for liver function and routine red cell observations, it should be possible to detect the earliest signs of T.N.T. poisoning in time to remove the worker from his dangerous environment, and early enough to institute treatment by the administration of glucose, insulin and vitamin *C*, which hastened the recovery of five of Evans's patients.

PERFORATED PEPTIC ULCER AND HEAVY AIR RAIDS.

THE influence of the nervous system on the occurrence of peptic ulcer is generally recognized and has often been mentioned in these columns. In view of this known association it would be expected that mental stress and anxiety caused by war conditions would either increase the incidence of ulcer or aggravate the symptoms caused by it. That such a view is correct has been shown in a recent study[2] by D. N. Stewart and D. M. de R. Winser, medical students at Charing Cross Hospital, London. They state that shortly after the beginning of the second week in September, 1940, when serious raiding on London began, seven patients with perforated peptic ulcers were admitted within a few days to Charing Cross Hospital, which normally admits one a month. They set out to discover whether this increase was more than a chance one. They quote figures from the Registrar-General to the effect that deaths from peptic ulcer during the second year of war increased by 28% for men and 22% for women. They approached eighteen other London hospitals and asked permission to examine the records from 1937 to 1940. It is on the information gathered in this way that their conclusions are based. The average number of perforations per month was 25; for September and October, 1940, the average was 64. The increase is considered statistically and shown to be significant. The possible causes for this significant increase that were considered included acidity, vascular changes, miscellaneous drugs, trauma, bacteria and nervous strain. These are discussed in turn. Acidity and vascular changes and miscellaneous drugs are dismissed. It is admitted that possibly hard food, hastily swallowed meals, and an increased consumption of alcohol and tobacco may all have helped in causing the increase. In discussing bacteria as a cause, the authors point out that air raid shelter life would have given an infective factor good opportunities to operate. Lord Horder, however, is stated to have declared that in those times the country's health was particularly good. There was also a drop in the number of perforations during two months when the shelters were as well patronized as ever. This leaves only a nervous factor. Here Stewart and Winser quote many investigators who have produced experimental and clinical evidence regarding the relationship between a nervous factor and peptic ulceration and perforation. The conclusion that the probable cause for the increase in perforation of peptic ulcer was anxiety will be accepted. Stewart and Winser refer most aptly to the passage quoted by Alvarez from the Book of Proverbs: "Better is a dry morsel and quietness therewith than a house full of feasting and strife." An investigation such as this, in addition to having a scientific interest, can be used to point a moral to the people about their morale.

[1] *The Lancet*, November 8, 1941.
[2] *The Lancet*, February 28, 1942.

SPECIFIC GRAVITY AS AN INDEX OF OBESITY.

THAT the specific gravity of the body as a whole is close to that of water is known to every swimmer. To determine the specific gravity of the tissues alone it would be necessary to make amongst other corrections one for the air contained in the lungs. In an interesting research some medical officers of the United States Navy have made use of specific gravity as an index of obesity, for adipose tissue has a density of 0·94, the only tissue with a density less than that of water.[1,2] It is obvious that in obese persons the specific gravity will be low, in lean persons high. These American investigators used the principle of Archimedes—that is, the whole body was weighed in air and weighed again immersed in water, a heavy lead belt facilitating submergence. The crux was to allow for the pulmonary air. This they did by measuring the residual air by the helium-oxygen method and weighing the body during maximum pulmonary deflation. It is suggested that a specific gravity of 1·060 should be taken as critical, all registering below this to be regarded as obese and unfit for service in armed forces. This criterion, it is found, gives different and, it is claimed, better results than the height-weight tables. Two criticisms may be levelled against this technique; both are indeed mentioned by the authors but not properly dealt with. One is the presence of gas in the abdominal viscera. To minimize this error the determinations were made in the morning on the fasting subject, but the authors forget apparently that the colon may remain undeflated until after breakfast. The second source of error is the variable mass of bone in the skeleton, and bone has a high specific gravity. In future experiments methods may be devised to make proper allowance for this latter variable.

APPRECIATION FROM THE AUSTRALIAN IMPERIAL FORCE.

THE commanding officer of a field ambulance in the Australian Imperial Force abroad, in the course of a letter to the Editor of this journal about one of his officers who had been transferred to another unit, has given additional proof of the value of medical journals to medical officers of the armed forces serving overseas. He closes his letter with the following paragraph:

Ever since leaving Australia in 1940 it is pleasing to record the regularity with which I have received my copies of the Journals, and I have found them more than ever helpful and informative, and I know this to have been the position with my fellow officers.

[1] A. R. Behnke, junior, B. G. Feen and W. C. Welham: "The Specific Gravity of Healthy Men", *The Journal of the American Medical Association*, February 14, 1942, page 495.
[2] W. C. Welham and A. R. Behnke, junior: *Ibidem*, page 498.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Plastic Repair of Deformities of the Eyelids.

A. LLOYD MORGAN (*The Canadian Medical Association Journal*, June, 1941) writes on the plastic repair of deformities of the eyelids. In his opinion plastic surgery around the eye should be considered the province of the ophthalmologist. He describes the technique and discusses the special points in the plastic surgery of (*a*) cicatricial ectropion of the lower lid, (*b*) ptosis with epicanthus, (*c*) congenital coloboma of the upper eyelid.

Vitamin B Complex Deficiency in Retrobulbar and Peripheral Neuritis.

B. GOTTLIEB (*The British Journal of Ophthalmology*, December, 1941) presents a case of retrobulbar and peripheral neuritis brought about by vitamin *B* complex deficiency. The patient was a man, aged forty-six years, a publican, who for thirty years had been in the habit of taking considerable quantities of alcohol and of smoking about two ounces of "shag" tobacco per week. Since the beginning of the present war he had exceeded one pint of whisky per day and had smoked over three ounces of "shag" per week. His diet contained no green vegetables, except on rare occasions, no wholemeal bread, no raw vegetables, no pork and no liver; it consisted largely of white bread and butter, tea and cakes, with some meat and potatoes and fried fish (haddock or plaice). The vision of both eyes became impaired, so that at the time of his admission to hospital he was unable with the right eye to count fingers at a distance beyond two feet and with the left eye beyond one foot. The fundi were normal. Obvious bilateral central scotomata were present in the visual fields. No nystagmus was present. Signs and symptoms of peripheral neuritis were also present. He was treated with a full mixed diet and was given one ounce of "Bemax" three times a day by mouth and two milligrammes of vitamin B_1 by intramuscular injection every day. After one week he left hospital, but continued to have "Bemax" and vitamin B_1, a mixed diet and wholemeal bread. He was advised to give up alcohol, but continued smoking as before. Eight weeks after his admission to hospital vision in the right eye was 6/6 and in the left eye 6/18 partly. Later, the taking of some alcohol caused a recurrence of blurring of vision; he had in the meantime abstained from smoking tobacco. Nine months later he was in good health and no symptoms or signs of peripheral neuritis were present; vision in the left eye had improved to 6/7·5. A central scotoma for red was present in the left visual field, while the temporal half of the left optic disk was pale. The author points out that one important aspect of the case is that the symptoms and signs of retrobulbar and peripheral neuritis, which had been growing progressively worse, diminished in spite of the continuation of tobacco smoking; he suggests that this indicates that tobacco was of little or no importance in the ætiology, and proceeds to discuss the literature of the subject. He concludes that alcoholic retrobulbar neuritis is probably due to a deficiency of vitamin *B* complex, possibly vitamin B_1, and that retrobulbar neuritis in pregnancy and in some cases of diabetes is probably due to vitamin B_1 deficiency. He suggests that all cases of bilateral retrobulbar neuritis should be investigated with regard to the vitamin *B* content of the diet, particularly if the lesion is associated with evidences of pellagra, beriberi or peripheral neuritis, and treated accordingly.

The Standardization of Treatment of Interstitial Keratitis.

JOSEPH V. KLAUDER AND ELEANOR VANDOREN (*Venereal Disease Information*, September, 1941) present an analysis of 532 cases of interstitial keratitis, with particular reference to the standardization of treatment. The patients, all of whom had congenital syphilis, were treated or observed for at least one year. Various plans of antisyphilitic treatment were evaluated in terms of the patient's visual acuity at the final examination. Patients with interstitial keratitis who also had cataract, glaucoma or primary or secondary optic atrophy were excluded from that part of the study concerned with the evaluation of treatment. Of the patients, 73% were white and 27% were Negroes; 60% were females. The average age at onset was twelve years for females and thirteen years for males. The blood serum of 30% of patients with inactive interstitial keratitis previously treated failed to react to tests for syphilis; the blood serum of 2·5% of untreated patients with active interstitial keratitis failed to react to such tests. In 532 patients other syphilitic manifestations were present in the following proportions: Hutchinson's teeth 40%, bone and joint involvement 35%, labyrinthine disease 10%, chorio-retinitis 8%, neurosyphilis (symptomatic and asymptomatic) 8%, paresis and tabo-paresis 0·4%. In 42% of patients both eyes were involved either simultaneously or within one month of each other; the percentage increased slowly to the tenth year, when the second eye had become affected in 79%. "Routine" treatment consisted of more than 20 injections of an arsenical or of less than 20 injections in conjunction with a heavy metal. The different forms of treatment were: "routine" treatment, "routine" treatment with iodides, "routine" treatment with fever (malaria, mechanical fever therapy or vaccines given intravenously) and "routine" treatment with iodides and fever. Treatment was continuous, intermittent or irregular. It appeared that treatment in the inactive stage of interstitial keratitis was of limited value in improving visual acuity. The authors emphasize the importance of giving at least 20 injections of an arsenical in the active stage of the disease; arsphenamine and neoarsphenamine gave approximately the same results. The administration of iodides unfavourably influenced final visual acuity in both active and inactive interstitial keratitis. "Routine" therapy supplemented with fever therapy was superior to other forms of treatment in preventing relapse. Relapse was more frequent after treatment with less than 20 injections of an arsenical than after treatment with more than 20 injections. Continuous treatment was superior to intermittent or irregular treatment only in so far as the final visual acuity of the poorer eye was concerned, and in causing less poor visual acuity or blindness. The best results were obtained amongst patients with active interstitial keratitis who were treated with an arsenical combined with the use of a heavy metal and fever therapy.

Traumatic Changes in the Fundus.

ARTHUR J. BEDELL (*The Journal of the American Medical Association*, November 22, 1941) presents a description of changes in the fundus due to trauma. The chief signs of ocular injuries are hæmorrhage, œdema, ischæmia and destruction of tissue; their amount, location and extent provide the unpredictable elements. The fundus patterns made by trauma are both numerous and destructive. Those resulting from loss of tissue are holes in the retina and ruptures of the chorioid; those from disturbed circulation include holes, macular pigmentations, chorio-retinitis and embolisms; the special inflammatory reactions are *retinitis proliferans* and scars. Actual cutting includes avulsion of the optic nerve, and the result of pressure on the nerve in the orbit, the bony canal or the brain is papilœdema or atrophy. Many injuries produce immediate visible changes, while others have delayed effects; therefore reexaminations are imperative. Holes in the macula can result from injury, from inflammation of the uveal tract or from disturbance of the retinal circulation. When one or more of these agents is present, great care must be exercised in the evaluation of the effect of trauma; the decision may be of medico-legal importance, and the maintenance of the delicate balance of justice must rest on the sure foundation of knowledge, not bias. A detailed description is given of the following conditions: traumatic hole in the retina, rupture of the chorioid, rupture of the retina, Berlin's œdema, embolism of the central retinal artery, chorioidal hæmorrhage, glaucoma, traumatic atrophy of the optic nerve, avulsion of the optic nerve, congenital coloboma; *retinitis proliferans*, traumatic macular pigmentation, traumatic chorio-retinitis, penetrating wounds, changes due to foreign bodies, detachment of the retina, choked disk and traumatic arachnoiditis. The author holds that an ophthalmoscopic examination is imperative in every case of injury to the head or the eye. Meticulous care should be taken in the original description of the lesions, special notes being made of the time interval, the type of injury, and if possible the direction of the force and the end result. No report is complete without a clear photograph. An attempt must always be made to determine whether the changes are traumatic or non-traumatic.

Recovery from Central Retinitis.

ROSA FORD (*The British Journal of Ophthalmology*, November, 1941) reports a case of central retinitis in which complete recovery followed drainage of the nasal sinuses. The patient, a girl, aged eighteen years, had a small patch of chorioiditis in the right fovea, which in three days reduced vision to less than 6/60. Four days after the onset in the right eye the left eye became affected, more severely than the right. No cause could be found for the condition and all investigations produced negative results. Remembering another case, in which visual acuity had been temporarily improved by a submucous

resection of the nasal septum undertaken on purely empirical grounds, the author determined to try the effect of sinus treatment; this was begun on the fourth day from the onset. Small pieces of wool soaked in hydrogen peroxide were placed in each side of the patient's nose and left for twenty minutes. She was also given three inhalations of friar's balsam and took six grains of an aloes powder each day. Improvement was rapid; within twenty-four days from the onset vision was 6/6 (every letter) in both eyes, and only the pigmented area in each fundus remained as a permanent scar. The patient continued the hydrogen peroxide and aloes treatment for two years, fearing to discontinue it. Her general health remained excellent, and seven and a half years later she had had no further trouble with her eyes and had successfully completed a college course. The prompt recovery following nasal treatment suggests that a septic focus in the sinuses was responsible for the condition. Further, the author points out that negative clinical and radiological findings are not conclusive with regard to infection in the nasal sinuses. She concludes with a warning that hydrogen peroxide packs are not suitable for all patients.

A New Instrument for Removing Foreign Bodies from the Eye.

JOSEPH B. BIEDERMAN (*The Journal of the American Medical Association*, March 7, 1942) presents a preliminary report on a new instrument for removing foreign bodies from the eye. The device consists of a plastic magnifier and a finely rounded magnetized wire loop, which in turn is attached to a magnetized metal plug. The magnifying portion is made of a plastic material so that it will not break when dropped. The smooth wire loop is magnetized so as to attract small metal particles embedded in the eye. Large deeply embedded metal particles will require the use of a larger magnet; but the small superficial particles can be removed with the instrument. Non-metallic particles are mechanically removed by the smooth wire loop.

Glioma of the Retina.

EDITH M. PARKHILL AND WILLIAM L. BENEDICT (*American Journal of Ophthalmology*, December, 1941) have made a histo-pathological study of 35 eyes enucleated on account of the presence of tumours of the retina. The ages of the patients at the time of operation varied between one and five years. A tumour was present in the left eye in 15 cases, in the right eye in 15 cases and in both eyes in four cases; in one case the situation was not recorded. Of the patients, 18 were males and 16 females; the sex of one was not recorded. The tumours were divided into two groups on the basis of differentiation of cells: (i) an extremely undifferentiated retinoblastoma type and (ii) a partially differentiated neuroepithelioma type. The results of treatment in the first group were poor in comparison with those in the second group. In the first group only two of the 16 patients traced had had good results from treatment; in the second group 10 of the 16 patients traced had had good results. Twenty of the total of 35 patients died within periods varying up to ten years after operation; of these 20, one patient, whose tumour was a neuroepithelioma, died from heart disease with no sign of recurrence or metastasis. From their study of the tumours the authors were able to draw a number of conclusions. They consider that neuroepitheliomata seldom, probably never, arise from the rod and cone cells of the retina. Gliomata of the retina of any type frequently arise in the inner nuclear layer, less frequently in the ganglion cell and nerve fibre layers, and rarely, if ever, in the outer nuclear layer. When regions of normal retina persist, the tumours frequently appear to be of multicentric origin. Retinal tumours probably do not arise from embryonic rests or from persistent primitive epithelium, but from normal cells that have dedifferentiated to produce tumour cells. The cells from which the tumours arise are probably almost always glial cells. The least differentiated tumour cells are the small cells with hyperchromatic polygonal or wedge-shaped nuclei that predominate in the retinoblastomata; they are extremely anaplastic and do not correspond necessarily to any known cell of normal retinal embryogenesis. Cells in rosettes are not rod and cone cells and are much less differentiated than rod and cone cells. The formation of rosettes is evidence of partial differentiation of the tumour cells to a point at which they resemble more or less closely the cells of the primitive neural tube. The formation of pseudo-rosettes also signifies differentiation of the tumour cells, probably almost to the degree attained by the cells of true rosettes. The alignment of cells resembling epithelial cells into rows and bands, sometimes surrounding blood vessels, is a further manifestation of a slight degree of differentiation.

OTO-RHINO-LARYNGOLOGY.

The Protection of Hearing.

E. D. DALZIEL DICKSON AND A. W. G. EWING (*The Journal of Laryngology and Otology*, July, 1941) have tested numerous appliances for protection from noise, and particularly aeroplane noise. The chief components of aircraft noise are those due to the engine and to the propeller. The frequencies giving the highest relative intensities were those between 30 and 200 cycles. Whereas the first noticeable deficiency in occupational or traumatic deafness is about 4,096 cycles, it seems difficult to avoid the conclusion that very intense sound of low pitch may be responsible for high tone deafness. To insulate the ears against sound of low pitch has proved, however, to be remarkably difficult. Much of the paper describes recent experiments made by writers to this end. The two principles followed by designers of ear defenders have comprised either occlusion or plugging of the external canal or covering of the whole ear or even the whole head. Whatever the method, the more complete the occlusion, the greater is the interference with capacity to hear speech. Groups of previously trained and untrained subjects were used to test the protection against a series of pure tones emitted by a loud speaker, and experiments were made with four of the already known most effective devices. The greater benefit obtained by previously trained subjects was apparent with all. Conclusions reached were that all devices are more effective against sounds of high than of low frequency. Also it was shown that ear plugs of more solid type give greater protection than plugs of lighter material or a leather pad fixed over the ears. It is pointed out, however, that where speed is necessary in fitting a device to the ears, some, though less efficient, are of value, especially for untrained subjects, on account of quick adaptability to the canal or pinna, and probably the leather pads can be more quickly fixed in place than any of the other kinds of device. Noises tests were also carried out with the most suitable ear plug as revealed by the pure tone tests and with flying helmets. Although each rendered noise more tolerable, deafness was not prevented. The use of plugs and helmet together improved the results, but after two hours' wear the helmet caused discomfort due to heating, nor was the measure of protection of the two together equal to the sum of either separately. Further, the degree of interference with perception of speech was such that the method is considered to be impracticable in actual flying. Summing up, the writers conclude that the most effective of devices tested are ear plugs of a solid but very pliable character capable of immediate adaptation to the size and shape of the individual meatus. Of the plugs best meeting these requirements, one has a metal core inserted in a soft rubber casing in such a way that an air space remains between the two materials. Another is a wax plug covered with a soft fabric, and as this plug becomes soft with body temperature it is capable of being moulded to the shape of the ear.

Acoustic Trauma in Man.

H. B. PERLMAN (*Archives of Otolaryngology*, September, 1941) discusses clinical and experimental studies of acoustic trauma in man. Audiograms of 30 persons who had suffered from exposure in their occupations are analysed into three groups: (*a*) those exposed to a single explosive sound, (*b*) those exposed to a rapidly repeated or continuous sound, and (*c*) those exposed to more slowly repeated discrete sound impulses. In all, the greatest hearing loss is in the higher tone scale, especially at 4,096 cycles. Experimental study to explain this 4,096 dip was undertaken by noting the effect of very loud pure tones on the threshold curve from a number of normal young adults. The subjects were exposed in groups to tones in octave ranges from 64 to 8,192 cycles, and at an intensity of about 100 decibels, which was just below the threshold of acoustic pain. After exposure of one hour depression of the threshold curve was usually found to be sufficiently lasting to permit repeated audiograms to be taken. Sound at 64 cycles produced no alteration in the threshold curves; 256 cycle sound produced variable effects. In those exposed to 512, 1,024, 2,048, 4,096 cycles depression of the threshold curve showed maximum effect, not at the same pitch as the tone employed, but one octave above it. Tinnitus, distortion of sound and diplacusis were noted in a proportion of the subjects during recovery. In attempting to reconcile the difference in form of depression of threshold curves obtained in the experiments with continuous pure tone stimuli and those found after exposure to explosive and various industrial noises, which produce typically earliest and greatest loss at 4,096, the author discusses analyses of explosive

sounds, such as from gunfire, and the enormous pressure waves associated with these. He also considers physiological and psychological experiments on fatigue and masking, and the possible influence of harmonics, but concludes that he is unable to explain the occurrence of maximum depression of threshold one octave above the frequency of the fatiguing tone as observed in his pure tone experiments.

The Relation of Infantile Mastoiditis to Infantile Mortality.

P. W. LEATHART (*The Journal of Laryngology and Otology*, September, 1941), in discussing the relation of infantile mastoiditis to infantile mortality, quotes figures from clinical experience and from the pathological department of the Royal Liverpool Children's Hospital. The author demonstrates a far greater incidence of mastoiditis complicating air-borne or food-borne infections in infants than is commonly recognized. In 72 post-mortem examinations of children having died of such infections, undiagnosed mastoiditis was found on one or both sides in 43, or 59·6%. During the same period 150 cases of mastoiditis were diagnosed and the patients were operated on with a recovery rate of 80%. Putting together the diagnosed cases of mastoiditis and those disclosed by post-mortem examination, the author shows that the percentage incidence of this complication in air-borne and food-borne infections reaches 60%. He suggests that it is even higher. The possible magnitude of mortality from this common oversight in infantile infections is stressed in the fact that of over 32,000 infant deaths *per annum* in England and Wales the majority were of the type classifiable as being the result of air-borne or food-borne infections. The plea is made that many of these deaths might be avoided with a timely diagnosis of mastoiditis and operation. Diagnosis may be overlooked owing to the infant's inability to demonstrate the seat of symptoms and owing to the fact that in the majority the tympanic membrane appears healthy. The first point is to be aware of the frequency of mastoiditis and so to suspect it in a case in which the patient's condition is not improving. A rise in temperature, an increase in head restlessness, crying as if in pain, and the appearance or increase of vomiting and diarrhœa suggest possible ear disease. Minor changes only may be noted in the tympanic membrane. Frequently nothing abnormal is seen. Palpable glands behind the sterno-mastoid muscle are a constant and valuable sign. Immediate operation is advised in all such cases and is simply and speedily carried out. Both sides frequently will have to be opened up. Prevention is discussed and is based upon the accepted anatomical fact that in children the Eustachian tube readily admits matter from the throat. Feeding should never be permitted while the patients are lying down; they should be constantly propped up and turned from side to side, and should never be permitted to lie on the back for any length of time.

Primary Tuberculous Complex of the Middle Ear.

H. A. BARR AND R. EVANS (*The Journal of Laryngology and Otology*, May, 1941) take pains to explain that in the case described by them the tuberculous *otitis media* forms the first focus of infection in the body and is tuberculous from the outset and is not a secondary infection superadded to a previous coccal suppuration. That the middle ear is susceptible to inoculation with the tubercle bacillus is supported by Fraser's experimental production of tuberculous *otitis media* in guinea-pigs by injection through the tympanic membrane. Since such a route is unlikely in the human patients it is assumed that infection takes place by way of the Eustachian tube, which in infants is widely patent. Vomiting with regurgitation of infected food is possibly the mode of introduction of the bacilli to the middle ear. Ghon's classical study of the developing tuberculous lesion is quoted by the authors, and his showing of the almost simultaneous development of the caseating focus and enlarged and caseating lymph nodes is drawn upon by them for demonstration of the mode of behaviour of a primary focus and the designation of this bilocal reaction as the primary complex. Such a complex, together with the absence of evidence of tuberculosis elsewhere, should be demonstrated in cases regarded as examples of primary tuberculosis of the middle ear. All patients described have been young babies. The authors' case is the eleventh described in the literature. In their patient discharge from the middle ear and swelling of the sub-auricular and post-auricular glands on both sides were noticed in the second month after birth. Bilateral mastoidectomy revealed extensive bony necrosis. The Mantoux test gave a positive reaction. The patient died about two months later with gastro-intestinal and respiratory tract symptoms. Post-mortem examination revealed enlarged glands along the sterno-mastoid muscles, the greater enlargement being in the upper part of the chain. A few miliary tubercles were found in the lungs and the tracheo-bronchial glands were only slightly enlarged. There were some miliary tubercles in the spleen. No other focus which could have been primary was found. In the temporal bone and cervical lymph nodes well-developed tuberculous changes were evident on microscopic examination. Tubercle bacilli were fairly numerous in caseated upper cervical glands, but only a few were found in the mesenteric nodes and none elsewhere. Only in relation to the middle ear and upper cervical glands could a Ghon's focus be found. The prognosis in such cases is very serious; in 10 out of the 11 cases reported the patients have died in infancy. The authors believe that the seriousness of the condition justifies radical operation, as this offers the only hope for removal of the focus before blood-borne infection becomes generalized.

Fenestra Nov-Ovalis: A New Oval Window for the Improvement of Hearing in Cases of Otosclerosis.

JULIUS LEMPERT (*Archives of Otolaryngology*, November, 1941) states that during the past three and a half years he has operated on 375 patients suffering from otosclerosis. In 300 of the cases the one stage endaural technique devised by himself has been employed. In 88 of these the artificial fenestra in the external semicircular canal eventually became closed, either partially or completely. Opportunity to seek some visible explanation of this presented itself when a patient died of coronary thrombosis fourteen days after operation. Photomicrographs from this case revealed the presence of some blood clot and fibrous connective tissue formation within the perilymph space, and some binding down of the endolymphatic labyrinth by the latter. Inspection of the obstructed fistula in other cases at revisionary operations always revealed fibrous tissue formation, but no fresh bony growth from the margins of the fenestration. A gradual increase in this fibrous plug and in time a tendency to undergo bony metaplasia were noted in those patients who were left untouched and were observed over longer periods. The greater change was found in those cases in which the opening had been made farthest from the ampulla, and in those in which closure was incomplete the remaining fistula was always nearest the ampulla. From these observations the author has reasoned that blood clot in the perilymph space may lay the foundation for fibrous tissue formation, and that it is on account of the relatively shallower canal, as compared with the deeper ampullary region, that the coagulum remains unabsorbed and may make contact with adjacent parts and thence progress to fibrous tissue formation. It was also realized that the epithelium-lined Shrapnell's membrane might more often reach and cover an opening nearer the ampulla, whereas only the adjacent periosteum-covered lining from the external auditory canal might cover those portions of the fenestra further back along the external semicircular canal, when the plastic flap devised by the author was turned back to cover the fenestra and mastoid cavity. In the last 75 cases of his series the author has made a larger opening above the facial ridge through the dome of the vestibule, exposing the utricle. Here there is exposed a perilymph space, according to Gray, having a depth of three millimetres, a height of five millimetres, and five millimetres in length, as compared with a depth of only 0·8 millimetre of the perilymphatic space of the external semicircular canal. With the use of a plastic flap cut from the lining of the external auditory canal and directly continuous with the mobilized tympanic membrane, it is possible to cover completely the newly placed vestibular fistula made through the bone by the epithelium-lined and extremely thin Shrapnell's membrane. Other points in technique are believed by the author to be responsible for his successful results. Thus the opening is first made by means of a dental polishing burr. The bony margins, including the inner cambium layer, are then enlarged and smoothed with fine dental spoon elevators. Finally the walls are smoothed and polished with a 24-carat gold burnishing burr. It is believed that in this manner the Haversian canals are closed and the likelihood of bony growth is reduced. Careful washing with warm normal saline solution to remove bony particles is necessary. The perilymphatic membrane is next removed by needling and further washing. Time is allowed to assure that all bleeding has ceased and then the flap is placed carefully in position. The author publishes audiograms from a number of cases in which operation by this method was adopted. It is claimed that so far, after intervals of up to eighteen months, in no case is there evidence of occlusion of the newly placed labyrinthine fistula. As a further assurance against closure the author is experimenting with a metal obturator of iridio-platinum.

PATHOLOGY.

Changes in the Brain in Pertussis with Convulsions.

THE changes in the brain in pertussis consist, according to V. B. Dolgopol (*Archives of Neurology and Psychiatry*, September, 1941), of œdema, ischæmic cellular degeneration, multiple hæmorrhages (usually small) and lymphocytic plugs in veins and capillaries. They are apparently non-infectious and most likely of circulatory origin. On rare occasions a secondary "encephalitic reaction" may be observed in addition to the aforementioned changes. It seems that the term "pertussis encephalopathy", proposed by Jochims, covers most adequately these conceptions and, in the present state of knowledge about the pathogenesis of lesions of the brain in pertussis, should be the term of choice for the cerebral complications in that disease.

Cavities in the Silicotic Lung.

ARTHUR J. VORWALD (*The American Journal of Pathology*, September, 1941) summarizes the pathological features and associated clinical picture of three types of cavities commonly encountered in the silicotic lung. Typical tuberculous cavity formation develops most often in persons with minimal silicosis. It is characterized by the ordinary pathological and clinical features of excavation in uncomplicated chronic phthisis. In the massive fibrotic lesions of tuberculo-silicosis, produced by the combined local action of silica and tubercle bacilli, cavities of modified form usually develop. They differ in morphology from the simple tuberculous cavities and do not give rise to the usual symptoms until the disease has existed for a very long period. Anæmic cavities also may occur within massive lesions of conglomerate fibrosis without evidence of active infection. They are probably due to local deficiency in blood supply, although the toxic action of high concentrations of silica may play a part. Of themselves, they do not cause recognizable clinical symptoms.

Appendiceal Oxyuriasis.

L. L. ASHBURN (*The American Journal of Pathology*, November, 1941) reports that in a series of 2,317 surgically removed appendices, oxyurids were found in 184 (7·94%). Seventy-nine were positive in the sectioned material, and in 105 oxyurids were found only by examination of the removed appendiceal contents. Of the 34 appendices showing oxyurids in section and having fæcal material in all three blocks sectioned, only one level was positive in 23 cases (67·65%), two levels were positive in seven (20·58%) and all three levels were positive in four cases (11·76%). The highest incidence occurred in the seven to eleven year age group, being (for the entire series) 15% for males and 22·22% for females. The decrease in incidence was gradual until the thirty-two to thirty-six year period, at which a second peak occurs—7·44% for males and 15·96% for females. Appendiceal infestation is rare after fifty-one years of age. Infestation is more common in appendices from females than from males. For the two to forty-six year age period the ratio is 1·0 male to 2·34 females. Comparison of infested and control ("negative") appendices showed that local eosinophilia is not significantly increased by infestation with oxyurids. Oxyuriasis occurs as frequently in normal appendices as in appendices showing chronic inflammation and more frequently than in acutely inflamed appendices. Of the 79 cases showing oxyurids in the lumen of the sectioned appendix, 13 showed the worm in contact with mucosa; seven of these showed pressure atrophy of epithelium with formation of shallow crescent-shaped depressions. Rarely there was a little karyorrhectic necrosis, but no inflammation or hæmorrhage was found. One appendix showed an oxyurid in the deep part of the mucosa. The lack of inflammation, necrosis or hæmorrhage shows that the invasion occurred after operation. No case of "*appendicitis oxyurica*" occurred in this series. Ashburn therefore ends with the statement that *Enterobius* (*Oxyuris*) *vermicularis* is not ætiologically related to appendicitis.

Tissue Reactions in Fatal Streptococcus Hæmolyticus Infection.

G. K. MALLORY AND C. S. KEEFER (*Archives of Pathology*, September, 1941) have studied the various tissues in fatal cases of hæmolytic streptococcal infection beginning as scarlet fever, erysipelas, wound infection or puerperal infection, and have found that anatomical changes were present in the heart, kidneys, liver, spleen, lungs and pancreas. The lesions in the heart and kidneys were studied in detail. In the heart the most common lesions consisted of focal accumulations of cells, composed for the most part of lymphocytes and plasma cells. Sometimes polymorphonuclear leucocytes and eosinophile cells were also present in varying numbers. In rare cases, in which the infection was acute and fulminating, lesions having the same distribution and localization, but consisting of organisms alone, organisms *plus* an acute suppurative reaction, or an acute suppurative reaction alone were found. The more common lesion, which is apparently the later stage of the lesion just described, was seen most often in patients who died between the sixth and fifteenth days of their illness. The degree of these reactions also was greatest at this time. The reactions were more conspicuous in patients with bacteriæmia, especially when such patients survived longer than ten days. From these studies it is suggested that the anatomical lesions were due in part to an antigen-antibody reaction. The anatomical distribution of the lesions also suggests an explanation for the late non-suppurative phenomena which are not infrequently found clinically following hæmolytic streptococcal infections. A possible relationship between these lesions and Aschoff bodies is also suggested.

Insufficiency of the Aortic Valve due to Syphilis.

DISSATISFIED with the generally accepted explanations of the syphilitic distortion of the aortic valve and ring, R. S. Jason (*Archives of Pathology*, September, 1941) has studied a series of 27 syphilitic hearts, including gradations from chronic to fulminating lesions. He found aortic valve distortions falling outside those commonly described, which could not be accounted for by the generally accepted explanations of pathogenesis. All of the valve distortions studied appeared to have been due to two processes: (*a*) a destructive inflammation of the aortic wall resulting in destruction and dislodgement of the cusp attachments at the commissures, and (*b*) a reparative fibrosis. These two processes, destructive inflammation and reparative fibrosis, are set forth and discussed as the basic factors in the genesis of aortic insufficiency due to syphilis. Support for the idea that destruction of tissue plays a significant part in the production of syphilitic valvular distortions is found in the partial reproduction of such distortions by dissection of normal valves.

Effect of "Cellophane" Perinephritis on the Granular Cells of the Juxtaglomerular Apparatus.

THE increased number of certain fuchsinophilic granular cells in the juxtaglomerular apparatus in rabbits made hypertensive by partial ligation of the renal artery has been interpreted as indicating that these cells may secrete a renal pressor principle. If these granular cells are the source of some constituent of the renin-vasopressor-inhibitor system, their behaviour should be similar in all instances of experimental renal hypertension, however produced. And their behaviour should be in accord with the recent work indicating an increase of renin and a decrease of inhibitor in hypertensive animals. Since there has been no report on the granular cells in hypertension produced by "Cellophane" perinephritis (method of Page), F. W. Dunihue (*Archives of Pathology*, August, 1941) has undertaken a study of these cells in this type of hypertension and the time relations of their behaviour compared with those of the reported assays on renin and inhibitor in hypertensive animals. He finds that in "Cellophane" perinephritis the granular cells of the juxtaglomerular apparatus are increased as early as the third day after the application of "Cellophane" to the kidney. These cells attain their maximum development in granularity, number and distribution prior to or simultaneous with the onset of hypertension and then subsequently decrease in number, but probably are never reduced to normal values. It is believed that the behaviour of these cells is consistent with the suggestion that they are the source of renin. It is suggested, however, that the secretions of these granular cells may render the vascular apparatus hypersensitive to pressor stimuli, which may be either chemical or nervous in nature.

Adenomatous Hyperplasia of the Adrenal Cortex associated with Essential Hypertension.

FOR several years J. F. Rinehart, O. O. Williams and W. S. Cappeller have been impressed with the frequent occurrence of hyperplasia of the adrenal cortex in association with essential hypertension. The result of a detailed anatomical study of the adrenal glands in cases with and without hypertension which they have undertaken (*Archives of Pathology*, August, 1941) is that nodular or adenomatous hyperplasia of the adrenal cortex is almost regularly found in association with essential hypertension. The cells are hyperplastic and many show a high lipoid content. Comparable changes are infrequent in adrenal glands from non-hypertensive patients. On the basis of this finding and other evidence cited, it is suggested that hypersecretion of the adrenal cortex may in some cases be a factor in the genesis of what is now classified as essential hypertension.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on October 23, 1941, at Saint Vincent's Hospital, Sydney. The meeting took the form of a number of clinical demonstrations by members of the honorary medical staff of the hospital.

Bone Pegging of an Ununited Carpal Navicular Bone.

DR. EDWARD G. MACMAHON showed a male patient, aged twenty-six years, an electrician, who in October, 1939, had fallen down a ship's hold, sustaining a compression fracture of the first lumbar vertebra. He was treated in a plaster jacket and was discharged from hospital three weeks later. Nearly three months had elapsed before it was discovered that he had also sustained a fracture of the right carpal navicular bone. The right wrist and forearm were then immobilized in plaster of Paris. Union failed to occur, and in July, 1940, the bone was drilled by the closed method under the fluorescent screen. Further relays of plaster of Paris were applied until May, 1941. There was still no sign of union, and it seemed that no useful purpose could be served by further immobilization, so the use of plaster of Paris was discontinued. Pain in the wrist persisted, however, with limitation of movement in all directions. Power was impaired and movement and jarring of the thumb aggravated the patient's discomfiture. He was unable to work. It was then that he came under Dr. MacMahon's care.

On July 14, 1941, under general ether anæsthesia, a longitudinal incision, two and a half inches long, was made along the dorso-lateral aspect of the right wrist. The navicular bone was exposed. A drill hole three-sixteenths of an inch in diameter was made through the navicular bone, passing across the line of fracture, and along this hole a bone peg fashioned from the right tibia was driven. The wound was closed and immobilization was secured by means of a plaster slab and multiple strips of zinc oxide strapping. At the time of the meeting three months had elapsed. The bone peg was in place, but the line of fracture was still visible. It was intended to immobilize the wrist for a further three months.

Lobar Pneumonia Complicated by Lung Abscess.

Dr. MacMahon also showed a seaman, aged forty-three years, who had been admitted to Saint Vincent's Hospital on March 30, 1941, complaining of a cough with faintly pink sputum, present for two weeks. He had experienced pain in the right side of his chest for three days; it was worse on breathing.

On his admission to hospital his temperature was 101·6° F., his pulse rate was 98 per minute and his respirations numbered 34 per minute. There was diminished respiratory excursion at the base of the right lung, with dulness and bronchial breathing. A diagnosis of lobar pneumonia was made and the patient was treated accordingly. He was given the usual course of sulphapyridine tablets. His temperature was normal on April 2 and 3, but on April 4 it again rose to 100° F.; the evening rise persisted. The radiographer's report on an X-ray film taken on April 4 stated that fairly extensive pneumonic consolidation was present over the lower half of the right lung field, with an extension to the middle zone of the left lung field. Further X-ray pictures taken on April 16 and 29 revealed regression of the area of consolidation, but in the latter film there was a suggestion of a small collection of fluid at the extreme base of the right lung. By May 9 this had extended, and on May 20 the formation of a central cavity with fluid level and air bubble was apparent. A lung abscess had formed. Clubbing of the finger tips was present and the temperature was now swinging up to 102° F. Postural drainage was carried out, with some improvement in the patient's condition, and on June 26, under local anæsthesia, an incision five inches long was made over the postero-lateral aspect of the eighth right rib. About three and a half inches of the seventh, eighth and ninth ribs were removed. The underlying lung tissue was adherent to the chest wall. The abscess cavity was opened and the outer wall removed with a soldering iron. About seven ounces of inspissated pus and a free piece of necrotic lung tissue were removed. Several small communications with a large bronchus were visible. The wound was packed with gauze. The high temperature gradually subsided, becoming normal on July 6 and remaining so. The patient was allowed up on July 9 and was discharged from hospital on August 1. He attended the out-patient department for dressings. At the time of the meeting his wound had healed, he had lost his cough, had gained over two stone in weight and was about to return to work.

Hæmatemesis Probably due to Aspirin.

DR. J. E. SHERWOOD showed a male patient, aged sixty years, who in 1921 had undergone an operation for pyloroplasty and gastro-enterostomy for duodenal obstruction. Ten years later, in 1931, a jejunal ulcer necessitated a further operation, when a large mass was found—probably inflammatory in origin—surrounding the affected intestinal loop. The first gastro-enterostomy had to be left undisturbed and a further one was established. Later, the patient had recurring attacks of severe hæmatemesis. In May, 1939, gastroscopy revealed gastritic changes of a superficial and atrophic character, suggesting gastritis of the post-operative stomach as the cause of the hæmatemesis. It was noticed that each hæmatemesis was preceded by an "influenzal attack". Accordingly he was advised to take to his bed with the first onset of such symptoms. The attacks of hæmatemesis still persisted. It was next found that he always took aspirin when each influenzal attack occurred. This was forbidden. Eighteen months had elapsed since then, and though he had had influenzal attacks, he had had no more attacks of hæmatemesis and no more aspirin.

Neurogenic Dysphagia.

Achalasia of the Cardia.

Dr. Sherwood's next patient was a woman, aged forty-seven years, who had complained of pains in all her joints over a period of years. On further questioning it was discovered that she had suffered from dysphagia with regurgitation of food for twelve years, and also from considerable dyspnœa on exertion. She had a previous history of malaria, but her past health otherwise appeared to have been satisfactory. She stated that previous X-ray examination revealed some œsophageal narrowing.

Examination disclosed a thin woman affected with pronounced rheumatoid arthritis. Clinical examination otherwise revealed no abnormality. An X-ray examination revealed typical achalasia of the cardia. Treatment was carried out by dilatation with Hurst's mercury bougies, with such relief to the patient that she had unfortunately returned to north Queensland.

Dysphagia of Cortical Origin.

Dr. Sherwood then showed a male patient, aged fifty-eight years, who complained of difficulty in swallowing hard foods, of two years' duration. His wife stated that for the same period of time he had suffered from loss of memory and mental deterioration. During the preceding two months he had had difficulty in swallowing even soft foods, and at the time of examination all food seemed to stick in the upper part of his chest until relief was obtained by vomiting.

On examination his nutrition appeared satisfactory, and some dysarthria was noticeable. The pupils of the eyes were equal and reacted to light and accommodation. The deep reflexes were active; there were no signs of ataxia in the form of Rombergism. The Wassermann test produced no reaction with the patient's blood serum. An X-ray examination of the thorax and œsophagus failed to reveal any abnormality. Small doses of iodide together with a little encouragement soon remedied the dysphagia, which was apparently of cortical origin.

Gastric Symptoms of Coronary Origin.

Dr. Sherwood's next patient was a man, aged seventy-five years, who complained of periodic pain in his chest about thirty minutes after food; the pain continued for two hours and was relieved by an alkaline powder. There was no history of vomiting or loss of weight.

On examination slight mid-epigastric tenderness was present. A systolic murmur was audible over the precordium. The patient's blood pressure was 160 millimetres of mercury systolic and 60 diastolic. An X-ray examination of his œsophagus, stomach and duodenum revealed no abnormality. A fractional test meal examination also revealed no abnormality. An electrocardiogram revealed a low voltage curve, but no other abnormality. Dr. Sherwood said that he was inclined to attribute the patient's gastric symptoms to coronary sclerosis, a not uncommon occurrence at his age in the presence of such a history.

Calcified Hydatid Cyst.

Dr. Sherwood then showed a female patient, aged sixty-five years, who complained of pain and flatulence after food, of three or four years' duration; the pain had been worse

during the preceding twelve months. The symptoms had been intermittent in character. She had previously had two operations for hydatid cysts of the liver and stomach. The operation scar was visible and the edge of the spleen was palpable. The Casoni test produced a positive reaction. A differential leucocyte count showed that 3% were eosinophile cells. An X-ray examination revealed a calcified hydatid cyst of the left lobe of the liver causing a filling defect of the greater curvature of the stomach.

Hæmorrhoids and Malignant Disease.

The next patient shown by Dr. Sherwood was a man, aged sixty-three years, who late in 1940 had for two or three weeks complained of a frequent call to stool, accompanied by slight bleeding *per rectum*, due in his opinion to "piles", which were certainly present. He demanded removal of the offending "piles". When further investigation was suggested he disappeared for some months. When he reappeared, he had in addition been suffering from some epigastric discomfort and anorexia. Apart from the hæmorrhoids, clinical examination still revealed no abnormality. An X-ray examination revealed a probable malignant lesion of the sigmoid colon; this had since been confirmed macroscopically and microscopically after operation. The patient appeared to be progressing satisfactorily.

Dr. Sherwood remarked that such cases were not uncommon; but the moral was that hæmorrhoids were not always what they seemed, and often there was a secondary underlying (or overlying) cause.

Paget's Disease.

Dr. Sherwood then showed a man, aged sixty-nine years, who complained chiefly of insomnia. He was extremely deaf, and his vision was failing.

On examination the broad skull with prominent tortuous and thickened vessels was obvious. The blood pressure was 220 millimetres of mercury systolic and 100 diastolic. Thoracic kyphosis and scoliosis were present. There were multiple pigmented moles on the skin of the back. Bowing of the legs was present; the right tibia appeared sabre-shaped, probably owing in part to an old fracture of that bone. The X-ray appearances were pathognomonic of Paget's disease.

Gout.

Dr. Sherwood's next patient was a man, aged fifty-three years, who had fallen on his right elbow at sea in May, 1941. The elbow became swollen and painful shortly afterwards. About one week later his fourth right toe and fifth left toe became swollen and painful. The owner of these affected parts explained that all were probably affected in the same fall. He stated that the swelling of the elbow fluctuated, but that the two toes had remained constantly swollen.

On examination the presence of tophi in his left ear and the discharge of sodium biurate crystals through the skin of both toes rather discounted the compensatory nature of his lesions.

Polycystic Kidneys.

Dr. Sherwood then showed a female patient, aged fifty-two years, who in 1928 began to suffer from backache, which had persisted intermittently since then. In 1940 she had had hæmaturia, which had recurred on one occasion since. No frequency of micturition was present, but sometimes slight scalding was noted. She had a section performed for a fibroid condition of the uterus. Her family history had been uneventful. In February, 1939, she was examined at a hospital in Brisbane. X-ray films made with the use of "Uroselectan" revealed a typical polycystic kidney on the left side, retaining only fair function, while on the right side moderately severe pyelonephritis was present. The cause of the latter was not clear. Later, in 1939, she was reexamined at an Adelaide hospital. A pyelogram revealed ptosis of both kidneys. As the ptosis was definite and the pain was relieved if the patient was recumbent, Dr. I. B. Jose decided to perform nephroprexy, one side at a time. The left side was dealt with first, and the kidney was found to contain multiple cysts. These were ruptured, but the kidney could not be raised to the intended level owing to the limiting length of the ureter. At a later date the right side was dealt with; the kidney was found to have a few cysts only, and classical nephropexy was performed. In 1940 a blood urea estimation showed thirty milligrammes of urea per 100 millilitres of blood. The percentages obtained by a urea concentration test were 2·3, 2·3, 2·8 and 2·8.

Dr. Sherwood said that the patient was a small thin woman; both kidneys were palpable, and cysts were present in the left one. The blood pressure was 130 millimetres of mercury systolic and 95 diastolic. The heart appeared normal.

Silicosis.

Dr. Sherwood next showed a man, aged fifty-eight years, who had been a miner for fifteen years; he had worked in gold mines for five years and in copper mines for a further ten years. He had had pneumonia and pleurisy thirteen months earlier. For twelve months he had had a cough with sputum and had also suffered from dyspnœa. X-ray examination revealed silicosis.

Silicosis with Tuberculosis.

Dr. Sherwood finally showed a man, aged seventy years, who had worked in mines since the age of sixteen years. Gold, copper and bismuth mines had been included in his itinerary. For eleven years he had complained of a cough with sputum and considerable dyspnœa. A tuberculous lesion of the apex of the left lung superimposed upon silicosis was revealed by X-ray examination.

(To be continued.)

Correspondence.

ACUTE HÆMOLYTIC ANÆMIA FOLLOWING SULPHONAMIDE THERAPY.

SIR: In your issue of November 22, 1941, under "Current Comment", page 599, attention is drawn to the comparative rarity of acute hæmolytic anæmia following sulphonamide therapy. The statement is made that the number of such cases reported still does not total a score. The following is the report of a case which was under the care of Dr. Alan Smith, to whom I am indebted for permission to report it.

L.S., a female, aged three years, had acute tonsillitis with a temperature of 103° F. on July 7, 1941. She was given one-quarter of a seven and one-half grain tablet of sulphapyridine, and this dose was repeated six hours later and a third dose was given six hours after the second, but the mother stated that this dose was vomited, so that she probably did not have more than about four grains in all. Soon after the third dose she became intensely anæmic, jaundiced and had marked hæmaturia. When I first saw her about this time she was in a semi-comatose condition, and the prognosis appeared to be extremely grave. Dr. Eva Shipton, who examined her blood, made the following report on July 8, 1941:

> Red blood corpuscles, number 1,430,000 per cubic millimetre (unable to obtain sufficient blood for hæmoglobin value); white cells, number 18,000 per cubic millimetre. Varieties: neutrophile cells, 80% (14,400 per cubic millimetre); lymphocytes, 18% (3,240 per cubic millimetre); monocytes, 2% (360 per cubic millimetres); eosinophile cells. There is no evidence of leuchæmia.

The child was given a transfusion of ten ounces of blood by the drip method, and the report on the blood a few hours later was as follows:

> Red blood corpuscles, number 2,150,000 per cubic millimetre; hæmoglobin, 45%; colour index, 1·04.
>
> Characters: Size, some small forms; shape, regular; colour, some polychromasia present; inclusions, some nucleated red cells seen.
>
> The platelets appear to be normal in films.
>
> White cells, number 20,000 per cubic millimetre. Varieties: neutrophile cells, 74% (14,000 per cubic millimetre); lymphocytes, 22% (4,400 per cubic millimetre); monocytes, 2% (400 per cubic millimetre); eosinophile cells, 2% (400 per cubic millimetre).
>
> There is no shift of the neutrophile cells and there are no toxic changes in the cytoplasm.

The report on the examination of the urine, which had lost its macroscopic blood after the first transfusion, was as follows:

> Reaction, strongly acid. Sediment: A few red cells only and some epithelial cells. Numerous short cylindrical bodies somewhat resembling casts, probably composed of acid hæmatin.

Twenty-four hours after the first transfusion her general condition had improved; but she still looked very anæmic, and a second transfusion, again of ten ounces and by drip method, was given. The following day, as she seemed much better, she was not given a transfusion, but a blood count made the next day revealed that the number of red cells had decreased and the hæmoglobin value was lower than on the previous examination. The full count was as follows:

Red blood corpuscles, number 2,100,000 per cubic millimetre; hæmoglobin, 41%; colour index, 0·97.

Characters: Size, normal; shape, regular; colour, polychromasia ++++; inclusions: a few Howell-Joly bodies seen and one normoblast, and many stippled cells.

White cells, number 12,400 per cubic millimetre. Varieties: neutrophile cells, 45% (5,580 per cubic millimetre); lymphocytes, 42% (5,208 per cubic millimetre); monocytes, 12% (1,488 per cubic millimetre); eosinophile cells, 12% (124 per cubic millimetre).

Of the neutrophiles, seven are band forms and two myelocytes were seen.

Dr. Shipton made the following comment on this report:

The anæmia is apparently hæmolytic in character and there is no evidence of leuchæmia. The significance of the numerous polychromatic forms (reticulocytes) is difficult to assess, but a blood count in about forty-eight hours would tell whether the young cells are being retained in the circulation or broken down.

A third transfusion was given forty-eight hours after the second, and a fourth twenty-four hours after the third. These two transfusions were each of ten ounces and both were again given by the drip method. From this time on the general condition of the child appeared to be quite normal and her subsequent progress was uneventful.

Dr. Shipton's report on the blood condition on July 18 was as follows:

Red blood corpuscles, number 3,480,000 per cubic millimetre; hæmoglobin, 65%; colour index, 0·93.

Characters: Size, normal; shape, regular; colour, only a few polychromatic cells seen; inclusions, no stippling and no nucleated red cells seen.

The platelets appear to be normal in films.

White cells, number 8,800 per cubic millimetre. Varieties: neutrophile cells, 57%; lymphocytes, 38%; monocytes, 3%; eosinophile cells, 2%.

There is no shift of the neutrophiles and there are no toxic changes in the cytoplasm.

The final blood count on July 26, 1941, was as follows:

Red blood corpuscles, number 4,000,000 per cubic millimetre; hæmoglobin, 72%; colour index, 0·9.

Characters: Size, A few small forms present; shape, regular; colour, a few polychromatic forms only; inclusions, none.

White cells, number 6,400 per cubic millimetre.

For such an intensive hæmolytic anæmia to develop after giving about three grains of sulphapyridine might suggest that the condition was coincidental, but this is unlikely. A case such as this emphasizes the fact that it is not the quantity of the drug administered that is important, but the susceptibility of the patient, and this appears to be impossible to determine before commencing treatment. It also shows that sulphonamide therapy should be reserved for cases that are not likely to yield to other methods of treatment.

In contrast to the above, a case occurred recently where seven grammes, the equivalent of fourteen tablets, of sulphapyridine were given intravenously to a child aged nine years who was suffering from severe meningococcal septicæmia. The solution was intended to be given over a period of twenty-four hours, but from an oversight the whole amount entered the circulation within two hours. The only ill effect noticed was some cyanosis, and the child made an unexpectedly rapid recovery.

Yours, etc.,

P. L. HIPSLEY, M.D., Ch.M., F.R.A.C.S.,
Honorary Consulting Surgeon, Royal Alexandra Hospital for Children and Royal Hospital for Women, Paddington.

Sydney,
Undated.

PHYSICAL FITNESS AND EFFICIENCY.

SIR: Mr. Dupain having sent me a copy of his letter to you, criticizing my letter in the journal of March 28, I beg to write as a rejoinder, should you entertain further discussion on the subject.

First, I did not advocate fencing as a *sine qua non* for physical fitness. I certainly did suggest that, for people approaching middle age, who have the ambition to attain physical and mental fitness, and have the determination to work for it, fencing was the only sport which will lead to that desirable state.

Mr. Dupain is quite right in saying that fencing has no popular appeal, and that scoliosis, *talipes plani et cetera* are noted in fencers; but he forgets that such is only the case when taught by the professional fencing master. Professional sport, if I may quote, is not sport at all, but a branch of the entertainment business.

The professional teaches fencing in view of staging a display, even a theatrical display. Or he has to plan his teaching in such a way that the pupil is entertained, and is not made to believe that sound fencing is intricate to learn. The pupil receives so many lessons and is then let loose to take his place in competitions amongst seriously trained fencers. He has received no preliminary training, but is given to understand that any athletic training will enable him to enter at a fencing competition. He "fights by the light of nature and does what he can, no matter how unorthodox it may be, to beat his opponent". He fights but does not fence.

"Such people go to work without judgment, they let fly at random", they advance or retire without any notion of balance, time or distance. "Their parries are wide, weak or vicious, without any sense of touch; their attacks are uncertain, wild and incoherent." They have no knowledge of, and still less respect for, the international rules governing fencing. "They throw arms, body and legs into such awkward positions that muscular and skeletal deformities must arise, unless they throw fencing up in disgust before the harm is done."

Such things do not happen to the fencer who has been instructed, and trained, on scientific lines.

Yours, etc.,

ALFRED E. FINCKH.

Sydney,
April 20, 1942.

THE TREATMENT OF BURNS.

SIR: I do not wish to waste space or argue over a trivial matter, but a possible misapprehension regarding hospital policy should be corrected. In his interesting letter published in your columns of April 18, F. W. Simpson quotes an earlier letter of mine (February 28, 1942) as implying that the general practice at Sydney Hospital is to treat burns with *Unguentum Acidi Borici* (B.P.). But what I said was that it had been used for some time in the casualty ward for burns of the hands and fingers.

What he says about it seeming neither ideal nor rational may be true, but many of us have to treat these injuries at times and in places when "ideal" measures are not available, and boracic ointment and lint are available almost anywhere. As to rationale, it has been judged by the results it gives, which (for burns of the hands and fingers) are very good indeed.

Yours, etc.,

P. W. GILL, Captain,
Australian Army Medical Corps.

April 21, 1942.

THE SURGICAL TREATMENT OF HYPERTENSION.

SIR: In your comment on the surgical treatment of hypertension (THE MEDICAL JOURNAL OF AUSTRALIA, April 4, 1942, page 414) it is implied that all hypertension sooner or later becomes perpetuated by the development of permanent organic changes in the vessels of vital organs of the body. Since this statement is only partly true and may have derived from some earlier remarks of mine, I should be glad if you will allow me space to correct it.

The essential abnormality in all the common forms of hypertension is an increase in the tone of the arterioles throughout the body. This leads to a structural thickening of the arterioles, and it is widely believed that once this arteriolar "sclerosis" has occurred, the increased peripheral resistance assumes a structural or irreversible character. Experimental evidence does not support this belief. By measuring the increase in the rate of blood flow through a limb after exposure to warmth or after brief arterial occlusion, Prinzmetal and Wilson[1] and Pickering,[2] working independently, have shown that the arteriolar relaxation observed in the normal subject is matched by a similar degree of relaxation in the hypertensive. This relaxation was demonstrated in benign, malignant and renal hypertension in all stages of the disease. It therefore appears that the generalized increase in peripheral resistance which is the basis of hypertension remains reversible to the end.

When essential hypertension becomes irreversible, as it does in some cases, the reason is to be found in the appearance of an entirely distinct kind of vascular lesion, the so-called necrotizing arteritis, which is also a direct result

of hypertension, and leads in the affected vessel to destruction of the muscular coat and often to considerable stenosis of the lumen. These necrotic vascular lesions are essentially focal in distribution, and although they are scattered widely throughout the body the proportion of arterioles involved is evidently not high enough to contribute a structural element to the increased peripheral resistance. Their significance lies in the fact that they show a predilection for the kidney, for, as Goldblatt's work has shown, the kidney is peculiar in that it responds to ischæmia by producing a pressor substance which causes generalized arteriolar constriction and a proportionate rise in blood pressure. Essential hypertension may be said to become irreversible when necrotizing arteritis has affected enough renal arterioles to generate a secondary or renal hypertension and so to set in train the vicious circle, renal damage ⇄ hypertension. In the malignant form of essential hypertension this stage is probably reached early in the disease. In benign hypertension, excepting the rare cases which take a malignant turn, there is no evidence to indicate that it is ever reached at all, for necrotizing arteritis is absent and the arterioles show only those diffuse changes which do not appear to impair function. Until such evidence is forthcoming there is therefore no cause to abandon as hopeless the search for a satisfactory treatment for established hypertension.

Yours, etc.,

The New Medical School,
University of Sydney,
April 24, 1942. F. B. BYROM.

References.

(1) M. Prinzmetal and C. Wilson: "The Nature of Peripheral Resistance in Arterial Hypertension, with Special Reference to the Vaso-Motor System", *Journal of Clinical Investigation*, Volume XV, 1936, page 63.

(2) G. W. Pickering and M. Prinzmetal: "Experimental Hypertension of Renal Origin in the Rabbit", *Clinical Science Incorporating Heart*, Volume III, 1938, page 357.

THE PAINFUL SHOULDER.

SIR: The article "New Light on the Painful Shoulder" by Captain Michael Kelly in your issue of April 25, 1942, is an admirable exposition of a neglected topic, and Captain Kelly is to be congratulated on his assiduity.

I should like, however, to make a few comments, which have come to my mind on reading this interesting paper.

In the course of the past sixteen years, which have been devoted principally to rheumatological conditions, I have dealt with approximately 300 cases of painful shoulder, brachial neuritis and cervical fibrositis.

In 1929, in eight cases, I tried the local injection of 20 to 25 cubic centimetres of a 1-200 solution of "Novocain" into the trapezius muscles—giving the infiltration in either two injections of 5·0 cubic centimetres each or five injections of 5·0 cubic centimetres each. In three cases the pain was so great that the patient refused to repeat the procedure, in two instances there was a relief of pain which lasted for some weeks, two cases had a recurrence of pain within ten days or so, and one patient, a burly station owner, required whisky to revive him, and then disappeared, somewhat ungratefully ignoring to this day the financial obligation which my enthusiasm had imposed upon him.

Needless to say, I abandoned this procedure, because apart from the above-mentioned consideration, I came to regard it as being illogical and unscientific.

Concerning the painful spots in the trapezius, these were demonstrated to me in 1926 by the late Percy Wilde, of Bath, and are mentioned in his book published in 1921. As far as memory goes, I think he said that he had acquired this piece of clinical information about the beginning of the century from an osteopath.

Regarding the ruptured supraspinatus tendon, I have had only one case, and that resulted from a football injury. This condition, in civil life, must be fairly rare.

Calcified deposits in or around the shoulder joint I have encountered in less than a dozen cases, but all were aged over forty years. I may mention that every case of mine, without exception, is systematically X-rayed through each affected joint before any treatment is instituted, and I keep the skiagrams for reference.

Over 8% of individuals who show signs of arthritis in joints of the upper extremity will exhibit the areas of tenderness in the trapezius, depicted so well by Captain Kelly.

Professor Ludwig von Pap, of Budapest, tells me that this is a fibrositis of the trapezius, but I am convinced that the spinal nerve roots are affected by surrounding inflammatory conditions, and if the situation is untreated, the pain will occasionally subside after a period, varying from three to twelve months, but the result after a few years will be an osteoarthritis of the spine, with osteophytes, and a return of the symptoms. Even this can be cured, but it will take several months. Of course nothing save a hammer and chisel will remove the osteophytes.

Why I said previously that the infiltration treatment is illogical is because I believe that all these types of cases, save those due to recent injury, are the early manifestation of arthritis—pre-arthritic in some instances.

Arthritis is a general, and not merely a local, metabolic disturbance. The general arthritic diathesis may be caused by many factors—psychological, endocrine, dietetic, toxic and traumatic. Adequate treatment of one affected joint should take into consideration all of these factors operating throughout the body. My usual standard of so-called cure is complete relief of pain, improved, or full movement—according to the chronicity of the disease—and no recurrence of symptoms for at least five years. This, I believe, can be attained in 90% of cases if taken within twelve months of onset.

Infiltration treatment is probably very useful as a palliative, and in order to enable men to resume duty within a short period of time, but it does not seem to me to be a very much more rational measure than prescribing an aspirin for appendicitis.

There is, however, one type of case not infrequently encountered—the persistent cervical pain and trapezial ache of the anxiety-neurotic, with a repressed homosexual basis. These, since they are rarely diagnosed correctly, except by those with some psychoanalytic knowledge, go from one doctor to another, and have never a good word for any. Nothing, save a chance diversion of their fantasies, or a lengthy psychoanalytical investigation, to undergo which they have rarely the intelligence or understanding, will alleviate their symptoms. It occurs to me that possibly in these conditions injection therapy might not be so inappropriate.

In spite of the above remarks—written, I fear, rather hurriedly—I should like once more to assure Captain Kelly of my appreciation of his comprehensive study. In my experience the vast majority of practitioners has neither the time, interest, ability or equipment with which to handle these complaints at all intelligently.

Although they offer an increasingly wide scope, the neglect of these "rheumatological" diseases is an uncomplimentary reflection upon both medical profession and public.

Yours, etc.,

231, Macquarie Street,
Sydney,
May 1, 1942. E. HASLETT FRAZER.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 127, of April 30, 1942.

AUSTRALIAN MILITARY FORCES.

Australian Army Medical Corps.

The following officers are transferred: Captain N75290 N. M. Stewart, 20th February, 1942; and Captain (Temporary Major) T. D. Freeman, and retains the temporary rank of Major, 19th March, 1942.

The notification respecting the appointment of Captain (provisionally) W16650 T. L. Williams, which appeared in Executive Minute No. 232/1941, promulgated in *Commonwealth Gazette*, No. 279 of 1941, is withdrawn.

The notification respecting the appointment of Captain (provisionally) N278336 R. D. Condon, which appeared in Executive Minute No. 19/1942, promulgated in *Commonwealth Gazette*, No. 28 of 1942, is withdrawn.

Captain A. J. De S. Howard is appointed from the Reserve of Officers, 2nd March, 1942.

The following officers are appointed from the Reserve of Officers and to be Captains (provisionally): Honorary Captains A. C. Ward, 24th January, 1942; S. J. McCafferty, 1st February, 1942; and G. A. Thompson and T. L. Cooney, 2nd March, 1942.

To be Captains (provisionally).—Thomas Edward Waters, 14th March, 1942; Joseph Goldman and Ronald Victor Wallace Roberts, 27th March, 1942; Aubrey Godwin Liddelow, William Henry Rolph, William Emmet Spring, Henry Boyd Penfold, Francis Morrissey Moore and Robert William Creighton Kelly, 30th March, 1942.

To be Honorary Captains.—Angus McNeil, 24th February, 1942; Thomas William Wiley, 25th February, 1942; Victor Henry Cumberland, 2nd March, 1942; George Kenneth Vincent, 6th March, 1942; Arthur Edward McKenzie Reddel, Donald Waterhouse Oakley, 19th March, 1942; Noel Simon Solomons, 23rd March, 1942; and Ronald Keith Stockbridge, 24th March, 1942.

ROYAL AUSTRALIAN AIR FORCE.
Citizen Air Force: Medical Branch.

Air Commodore T. E. V. Hurley, C.M.G., V.D., is promoted to Temporary Air Vice-Marshal with effect from 1st April, 1942.—(Ex. Min. No. 62—Approved 29th April, 1942.)

Obituary.

LOUIS SCHAEFFER.

WE are indebted to Professor A. N. Burkitt for the following appreciation of the late Mr. Louis Schaeffer.

Louis Schaeffer, whose name was a household word to students of medicine in the University of Sydney since the foundation of the school, died on April 16, 1942.

As one who knew him for a period of thirty-five years, I can say, and my colleagues agree, that he was a man of most remarkable character and ability. It was his human qualities as well as his great abilities that specially endeared him to those who knew him best, the various professors and lecturers under whom he served.

Starting as a boy of fourteen years when the department was founded, he trained under Professor Wilson and finally developed into a first-class photographer and photomicrographer, but his abilities were many and varied, from his capacities in the care and handling of the epidiascope, the manufacture of lantern slides, the preparation of bones, to his abilities as a musician when he was secretary of the Metropolitan Band.

Combined with these all-round faculties were his human qualities, a kindliness in helping students, a capacity for understanding and getting the best out of those who worked under him, and a perfect understanding of the needs and requirements of his seniors in the department. Many are the worries that he saved professors and lecturers for whom he worked. One of the outstanding features of his life was the complete devotion to the medical school and the department of anatomy. It was said that "Louis", as he was known to the many generations of students, lived, worked for and thought only of the department. Most of his week-ends were spent in the department, and official hours meant nothing to him.

For many years he scarcely ever took a holiday, and only in later years relaxed a little; his musical talent also gave him some relaxation. Otherwise one's picture of him is of a man with one purpose only, to serve his beloved department, often at a run, night and day, Saturdays and Sundays.

To this picture we must add his vitality and an imperturbability in moments of stress. Such devotion and happiness in work over a period of more than fifty years mark out Louis Schaeffer as one of the exceptional and outstanding characters concerned with the building up of the medical school of the University of Sydney, even if his activities were confined to what at first might seem to be a humble role.

There are few men of his humanity and capacity in this world, and we his professors for whom he worked consider it a privilege and great good fortune that the department of anatomy had the good luck to possess such a man as senior laboratory assistant for so many years.

GEORGE LORD SAUNDERS.

WE regret to announce the death of Dr. George Lord Saunders, which occurred on May 1, 1942, at Lindfield, New South Wales.

WILLIAM ALFRED VERCO.

WE regret to announce the death of Dr. William Alfred Verco, which occurred on April 29, 1942, at North Adelaide, South Australia.

ARTHUR AUBREY PALMER.

WE regret to announce the death of Dr. Arthur Aubrey Palmer, which occurred on May 5, 1942, at Sydney, New South Wales.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Hughes, William Henry Childe, M.B., B.S., 1940 (Univ. Sydney), Lake Crescent, Teralba.
Smyth, John Justin, M.B., B.S., 1941 (Univ. Sydney), 615, Forest Road, Bexley.

Diary for the Month.

MAY 12.—Tasmanian Branch, B.M.A.: Branch.
MAY 20.—Western Australian Branch, B.M.A.: Branch.
MAY 22.—Queensland Branch, B.M.A.: Council.
MAY 28.—South Australian Branch, B.M.A.: Branch.
MAY 28.—New South Wales Branch, B.M.A.: Branch.
MAY 29.—Tasmanian Branch, B.M.A.: Council.
JUNE 3.—Western Australian Branch, B.M.A.: Council.
JUNE 4.—South Australian Branch, B.M.A.: Council.
JUNE 5.—Queensland Branch, B.M.A.: Branch—Joseph Bancroft Memorial Lecture.
JUNE 9.—Tasmanian Branch, B.M.A.: Branch.
JUNE 12.—Queensland Branch, B.M.A.: Council.
JUNE 17.—Western Australian Branch, B.M.A.: Branch.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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